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# A COMPARATIVE STUDY OF IMMUNIZATION

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A multiplicity of new methods have been introduced into the medical practice of the present generation. This is a natural result of advances in the science of medicine but is especially a concomitant of progress in other fields, e. g., transportation, communication and industry, whereby the marvels of the laboratory have rapidly passed into everyday practice. Medical marvels have ever a credulous reception; it is not surprising that much hasty translation of experimental results into clinical practice has been seen.

The pediatrician is confronted especially by numerous new methods of active immunization which commend themselves to him by virtue of scientific authority or by weight of popular propaganda. It is essential that he examine separately each method proposed and that his knowledge be adequate regarding both the theory and the results of clinical trial under experimental conditions before he proceeds with attempts at universal or even widespread immunization. Judgment must not be based on purely philosophic grounds, such as plausibility and analogy to established procedures. Obviously, all these methods of immunization are not equally acceptable, and for the purpose of judging their applicability in pediatric practice the newer methods should be weighed with respect to the older and better established procedures. For the purpose of comparison there are three essential criteria, effectiveness, usefulness and safety, by which each method should be thoughtfully studied.

## CRITERIA

*Effectiveness.*—It must first be shown that the procedure provides effective protection with reasonable certainty and that this continues over a satisfactorily prolonged period. This is frequently not easily demonstrable. In only a few instances can effective protection be demonstrated by laboratory tests. Immunity is dependent not so much on the presence of serum immune substances in the patient as on his

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ability to produce them and to be protected in response to exposure. It is obviously impracticable to subject a group of supposedly immunized patients to inoculation or to deliberate exposure to test their immunity. It is usually necessary to determine the protective effect of inoculation by statistically comparing the response to natural exposure in vaccinated and in control groups. There are obvious potential errors in this type of investigation, the chief of which is the lack of homogeneity in any experimental series of human beings. Individual differences in size, age, sex, constitution and environment are responsible for a variety of quantitative and qualitative differences in immune status, both natural and induced. Certain patients are highly refractory to inoculation, and some, on the other hand, seem to be insusceptible to infection even in the absence of specific immunity. Not only do human beings in an experimental series vary in their immune status, but there are differences in the amount and the virulence of the inoculum introduced by natural exposure. Even in large groups the subjects exhibit kaleidoscopic combinations of these variable factors.

A significant field test for the effectiveness of inoculation, in order that these many variables may be controlled, must comply with several prerequisites: Large groups, both vaccinated and control groups, of similar numbers must be selected for comparison. The morbidity in the control groups must be significantly high. Investigations should be carried out in the same locality at the same time. Only large deviations between vaccinated and control groups are significant. The statistical material must be above reproach.

The effectiveness of an immunizing procedure is, on the basis of adequate tests, capable of fairly accurate mathematical expression. It is important, however, for the physician to remember the biologic limitations of arithmetic. It is impossible to predicate the precise immune status, quantitatively and qualitatively, of a subject on a numerical factor of effective protection in a series.

*Usefulness.*—Immunization against a disease must be of sufficient value to the patient to compensate for the discomfort, risk, expense and bother of the immunizing procedure. For example, protection against smallpox is undoubtedly valuable, but chickenpox is generally so trifling that even an effective immunizing procedure would be of little worth. Effective protection against Asiatic cholera is valueless in an environment where it never occurs. Theoretically a child might be immunized against many different infections, but there is a practical limit to the number of immunizing procedures which can sensibly be carried out.

*Safety.*—The treatment of disease sometimes entails actual risks to the patient; these risks must be justified by the danger to which the disease subjects him. The production of active immunity during health

does not ordinarily justify risks of more than a minor order, and the discomfort or disability occasioned by the injection of vaccine and similar preparations should never be disproportionate to the value to the patient of the immunity produced. An appreciable chance of producing disease or death should suffice to discredit any method at present imaginable. Earlier experiences with vaccination against smallpox, as well as certain experiences at the present day, do, of course, give evidence of certain dangers, but these have been and remain entirely proportionate to the danger of the disease. None of the common communicable diseases are sufficiently prevalent or severe to be comparable to smallpox when it is uncontrolled through vaccination.

## APPLICATIONS

A certain balance must naturally be maintained between these criteria. A useful and effective method may justify some increase in the risk; a method of little usefulness and of uncertain effectiveness is, on the contrary, inconsistent with the slightest danger in its performance. The use of these criteria for the evaluation by the clinician of prophylactic procedures is best illustrated by a consideration of the measures in common use.

*Smallpox.*—Vaccination against smallpox is the oldest of these measures. The experience of well over a century demonstrates that it is reasonably effective and sufficiently useful to justify the various risks which have been shown to attend it. Its merit depends largely, however, on this wealth of experience, and it might be difficult hastily to assemble data nearly so convincing as the clinical observation of generations.

*Diphtheria.*—Active immunization against diphtheria has, similarly, the advantage of the observations regarding its value made over a period of years. In contrast, to some extent, to most other diseases, diphtheria produces its effect almost entirely by means of its toxin, and antitoxic immunity is more effective protection than can confidently be predicted for most other diseases. In spite of laboratory studies indicating the presence and the persistence of immunity, the most convincing evidence of the effectiveness, usefulness and safety of active immunization proceeds from the analysis of extended clinical observations. Experience has indicated the desirability of changes in methods and agents and has demonstrated the unsuitability of perfectly plausible modifications. Unpredicted dangers have been encountered and have pointed the need for additional safeguards. Constant revaluation of the methods in the light of changing conditions is unquestionably necessary. Immunization against diphtheria probably imitates closely the method of spontaneous immunization. Under urban conditions immunity is naturally produced in a majority of persons before maturity. Doubtless the

production of artificial immunity is increased and continually enhanced by natural immunization. This is not necessarily a unique advantage, but in the case of few other diseases is natural immunity the result of exposure without the production of active disease. It is difficult to predict the precise effect of a continued increase in artificial immunization on the mechanism of spontaneous immunization. One should not, furthermore, state too glibly a subject's exact immune state, without giving thought to the effect of massive exposure or of the possibility of a lapse in immunity with time because of changes in the subject or in his environment. The subject will always present unknown factors. It can confidently be said, however, that in the mass active immunization protects against diphtheria safely, usefully and effectively.

*Typhoid Fever.*—Immunization against typhoid by the injection of vaccine has been demonstrably useful under certain conditions. It is difficult to determine the exact protective mechanism which is thereby developed. Immunity is not demonstrable by any test except the results of a mass experience large enough to discount an occasional failure. The duration of immunity is variable, uncertain and unpredictable. In general the dangers are limited to unpleasant reactions, but more serious results have been described. In ordinary practice, especially among children, antityphoid vaccination should be advised only on the basis of individual considerations. In relatively few communities are conditions such that one should be subjected to the periodic repetition of injections which is necessary for continued immunity.

*Scarlet Fever.*—Experimental studies regarding the nature of scarlet fever made it appear likely that immunization against this disease could be accomplished in a manner analogous to that in which immunization against diphtheria is carried out, and it seemed reasonable to suppose that a similar degree of protection could thus be conferred. There is no doubt of the extreme usefulness of a method which would be productive of effective protection against this disease. A great many observers, however, have been deterred from the extensive employment of inoculation because of the severe reactions which are not uncommonly encountered. These reactions are, in general, not of a dangerous nature but are sufficiently unpleasant to make the method tolerable only if the resultant immunity is demonstrably effective. Regarding the effectiveness of the method there is considerable conflict of opinion. One is confronted by the fact that the analogy between scarlet fever and diphtheria has a great many discrepancies. The Dick test for immunity is certainly less reliable than and not truly comparable to the Schick test. Demonstrable immunity to the rash-producing toxin does not indicate a degree of protection against the specific streptococcus comparable to that conferred against the diphtheria bacillus through immu-

nization against diphtheria. Field studies of inoculation against scarlet fever are still inconclusive regarding both the degree and the duration of the immunity conferred. Many observers will concur in the opinion that inoculation against scarlet fever is permissible under experimental conditions and that it is perhaps desirable for special groups, such as the personnel of hospitals for patients with communicable diseases, but that its general use as a public health measure is contraindicated on the one hand by the prevalence of severe reactions and on the other by the uncertainty which exists regarding the degree and the persistence of protection.

*Whooping Cough.*—A method for the successful production of active immunity against whooping cough would be extremely valuable. After years of uncertainty regarding the precise value of pertussis vaccine for early treatment and for protection after exposure, especially prepared vaccines similar to those which are used in immunization against typhoid have recently been recommended for use in active immunization prior to exposure. The actual risk they entail is inconsiderable, but the large, repeated injections occasion some discomfort and are tolerable only if they produce a satisfactory immune response. The results of field tests regarding their effectiveness are at present conflicting, and although some evidence seems to indicate that a certain protection is conferred, other evidence is at variance with this indication. If one may trust the analogy provided by other infections in which immunity is produced by the injection of a suspension of killed organisms, it may be necessary to repeat the injections after a few years if it is desired to prolong immunity. Second attacks of whooping cough are not uncommon; this does not support the view that prolonged immunity can be conferred through vaccination. Whatever the effectiveness of protection, its duration is completely uncertain. This problem is further complicated by the fact that whooping cough occurs most severely in young infants, in whom the immune response is poor and for whom the practicability of vaccination and the probability of producing immunity are equally dubious. The continuation of experimental studies of this measure cannot be criticized, but there is little to justify an enthusiasm which would place immunization against whooping cough on a par with immunization against diphtheria as a measure which should be universally carried out in pediatric practice.

*Poliomyelitis.*—One may further exemplify the importance of these criteria by applying them to the recently proposed method for immunization against poliomyelitis. The usefulness of this procedure is indicated only by the severe nature of the disease and not by the actual extent of its occurrence. A serious question regarding the safety of the method can be raised from the standpoint of laboratory experience.

and the lack of safety seems to have been demonstrated in clinical application. The effectiveness of the method is conceivably demonstrable only by field tests of magnitude conducted over a long period. So far the evidence regarding the usefulness, effectiveness and safety of this method has been such as to contraindicate its clinical application.

*Tuberculosis.*—Immunization against tuberculosis has been proposed and to some extent has been carried out by the injection of attenuated tubercle bacilli. The usefulness of this method should be studied with reference to the demonstrable usefulness of other methods for the control of tuberculosis. Considerations of safety have not been entirely settled by previous experience. The effectiveness of the protection conferred by BCG is not readily demonstrable and is further complicated by theoretical disagreement as to whether the patient with an altered immune response to the tubercle bacillus is less susceptible or more susceptible to manifestations of the disease.

This brief consideration of the various methods of active immunization in current use illustrates the necessity for the clinician to maintain a cautious and inquiring point of view regarding the introduction of new methods. There is real danger that if the child is subjected to more and more of this sort of thing he may profit less and less. The number of such measures to which the average well child should be subjected has a practical limit. The pediatrician should be content to continue the use of the older and proved methods of immunization and to resist the rapid introduction of new methods, in brief, to "be not the first by whom the new is tried, nor yet the last to lay the old aside."

# PRESENT STATUS OF PREVENTIVE INOCULATIONS AGAINST WHOOPING COUGH

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With the present annual average of 200,000 reported cases and 5,200 deaths—a death for every 39 cases reported—whooping cough warrants the concerted attention of clinicians and health officers. Its prevalence depends on the high index of communicability and the profuse dissemination of pertussis bacilli before cardinal clinical symptoms are well established. With quarantine so frequently delayed until the contagious period has nearly passed, new cases are inevitable. As pertussis is fatal only during the first few years of life, preventive inoculations should be undertaken as early as active immunization is likely to result.

Since 1916 Danish investigators have used a pertussis vaccine which contains 10,000,000,000 bacilli per cubic centimeter. Although their total dose of 2.2 cc. failed to prevent the disease, "fewer whooping cough deaths occurred when the inoculations were completed before the disease broke out." [1]

To increase the dose appreciably without risk and possibly to enhance its potency, a modification in technic was instituted at the Evanston Hospital in 1926. To insure the antigenicity of the vaccine, each lot is prepared from five to seven freshly isolated hemolytic cultures. To eliminate allergic reactions and to prevent sensitization to the blood proteins of animals, which may be carried over when the vaccine is harvested, human blood is substituted for the blood of animals in the culture medium. Because the bacteria-free vaccine filtrate produced cutaneous reactions when 0.1 cc. was injected intracutaneously, the vaccine is not washed—nothing is discarded. To delay deterioration, it is kept refrigerated. A total dose of from 7 to 8 cc. was injected just under the skin of the upper arms of 394 selected, young nonimmune private patients between 1928 and 1932.[2] Four hundred and fifteen instances of probable exposure to whooping cough were reported. Thirty-four

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Read before the New York Academy of Medicine, Section of Pediatrics, Jan. 14, 1937.

1. Madsen, T.: Whooping Cough, New England J. Med. **192**:50, 1925.

2. Sauer, L.: Immunization with Bacillus Pertussis Vaccine, J. A. M. A. **101**:1449 (Nov. 4) 1933.

of the inoculated children were in intimate contact with the disease in their brothers or sisters. As far as can be ascertained, none contracted it.

Since 1932, Northwestern University Medical School has granted two biologic laboratories the authority to make vaccine according to detailed specifications, which for commercial reasons deviate somewhat from the original technic. Phase I (Leslie and Gardner [3]) bacilli are used in the production of vaccine for sixty days after their isolation; the medium contains only 10 per cent of human blood, and the Helber counting chamber is employed for checking the concentration after the vaccine matches the standard. The vaccine was not made available to physicians until the commercial form was found to confer immunity on a high percentage of children. No lot is released unless retests at the Evanston Hospital show it to be pure, sterile and of the proper concentration. The expiration date has been extended to one year. Although the vaccine is not refrigerated while in transit, laboratories, jobbers, druggists and physicians are cautioned to keep it cold.

The earliest age at which active immunization can be conferred has not been established. During the past few years more than 1,000 infants less than 2 months of age, at the Cradle, and in 1936 about 1,071 infants from 2 to 6 months of age, who are being observed by the health department of Chicago, received injections. Few children more than 3 years of age have been inoculated. Because 8 of the 17 children in whom pertussis developed more than four months after inoculation were over 3 years of age at the time of injection, a total of 10 cc. (in doses of 2, 4 and 4 cc.) is recommended after the third year of life. The second half-year of life is probably the best time for preventive inoculation. The average age at the time of injection is 8 months. The syringe and the needles are sterilized by heat—preferably in the oven. The cap of the vial and the site of the injection are cleansed with alcohol. Wet dressings or external heat are not applied locally. Prior to Jan. 1, 1937, a total of 3,974 infants and children had been inoculated with authorized commercial vaccine. Quillian [4] inoculated 97 children with 8 cc. of the vaccine. Subsequently, 4 were intimately exposed to the disease, and none acquired it. Daughtry-Denmark [5] advocated a total dose of 14 cc. of authorized vaccine or 7 cc. of double strength vaccine because she found 100 per cent complement fixation reactions when that amount was used. Twenty-eight of 150 children inoculated with 14 cc. were subsequently exposed to whooping cough; none contracted it.

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3. Leslie, P. H., and Gardner, A. D.: The Phases of Haemophilus Pertussis, J. Hyg. **31**:423, 1931.

4. Quillian, W.: Immunization Against Contagious Diseases of Childhood, J. Florida M. A. **22**:407, 1936.

5. Daughtry-Denmark, L.: Studies in Whooping Cough, Am. J. Dis. Child. **52**:587 (Sept.) 1936.

Other investigators have reported on preventive inoculations with pertussis vaccine prepared in various ways. The Mishulow toxin vaccine, used by Park,[6] is made from selected stock cultures grown on 30 per cent sheep blood—beef heart agar. The growth is washed off with physiologic solution of sodium chloride plus 1 per cent of phenol. The Wright method of standardization is used. A total dose of from 65,000,000 to 88,000,000,000 bacilli was injected into 613 children. Four contracted whooping cough from two months to two years later. Park observed "marked reduction in the number of cases among the children that were vaccinated . . . as compared with the unvaccinated controls. Pertussis prophylactic vaccination with potent vaccine and adequate dosage seems desirable."

Mishulow, Mowry and Orange[7] injected toxin vaccine into a group of nonimmune children and authorized vaccine for another group of similar children. An agglutination response was noted in 84 per

TABLE 1.—*Results of Preventive Inoculations Against Pertussis with Authorized Commercial Vaccine*

| | Total Dose, Billions | Number Vaccinated | Number Subsequently Exposed | Number Who Contracted Pertussis |
|---|---|---|---|---|
| Sauer | 80 | 3,974 | 219 | 17 |
| Quillian [4] | 80 | 97 | 4 | 0 |
| Daughtry-Denmark [5] | 140 | 150 | 28 | 0 |

cent of the former and in 55 per cent of the latter. They found that the average agglutinin response was, on the whole, proportional to the dose injected. Injected intracutaneously, smaller amounts of vaccine produced as much agglutinin response as the customary subcutaneous dose. Shorr,[8] however, said:

> The intracutaneous route of administration was quickly abandoned because of the marked local reactions and the large number of injections necessary to give a total anywhere approaching the proposed dosage. The largest single injection given intracutaneously was 0.2 cc., and the total amount did not exceed 1 cc. in any child.

Kendrick[9] used a once washed suspension containing 10,000,000,000 phase I pertussis bacilli per cubic centimeter grown on Bordet-Gengou

6. Park, W. H.: Pertussis Prophylactic Vaccination, Brit. M. J. **2**:253 (Aug. 1) 1936.

7. Mishulow, L.; Mowry, I., and Orange, R.: A Comparative Study of Agglutinin Response After Pertussis Vaccination with the Sauer Vaccine and with a Toxin Vaccine and in Untreated Clinical Pertussis, J. Pediat. **9**:492, 1936.

8. Shorr, B.: Prophylactic Pertussis Immunization, J. Pediat. **9**:49, 1936.

9. Kendrick, P., quoted in Round Table Discussion on Prophylaxis and Treatment of Whooping Cough, J. Pediat. **9**:117, 1936.

medium enriched with 15 per cent of sheep blood and 1 per cent of proteose peptone. The organisms were killed with a solution of merthiolate, 1 : 10,000, or a 0.5 per cent solution of phenol. The total dose of 7.5 cc. was divided into four weekly injections. The study embraced a total of 2,285 children, about half of whom were controls. Of 118 inoculated children who were subsequently exposed, 15, or 11.9 per cent, contracted pertussis. In the control group 149 were exposed and 111, or 88.1 per cent, contracted pertussis. Kendrick concluded: "Our study has not been carried on for a sufficient time nor do our results embrace sufficient numbers to warrant final conclusions."

Doull, Shibley and McClelland [10] published an interim report on a vaccine prepared from cultures of recently isolated phase I bacilli grown on modified medium containing from 25 to 35 per cent of citrated blood. After the growth was suspended in distilled water it was subjected to centrifugation. The supernatant liquid was discarded, and the sediment

TABLE 2.—*Results of Preventive Inoculations Against Pertussis with Vaccine Prepared in Various Ways.*

| | Total Dose, Billions | Number Vaccinated | Number Subsequently Exposed | Number Who Contracted Pertussis |
|---|---|---|---|---|
| Park [6] | 65-88 | 613 | ... | 4 |
| Kendrick [9] | 75 | 1,575 | 118 | 15 |
| Doull, Shibley and McClelland [10] | 80 | 422 | ... | 61 |

was resuspended in an 0.85 per cent solution of sodium chloride to which 0.5 per cent of phenol was added. A total dose of 8 cc. was injected into the buttocks of 482 infants who were being observed by welfare agencies at Cleveland. In two years 61 of them contracted pertussis. In the control group of 496 infants, 71 contracted pertussis. The vaccine of these workers, washed in distilled water, did not confer protection.

## COMMENT

Schick [11] defined immunity as "the ability of an organism to counteract, in a specific way, the damaging effect of a bacterium or virus so that no symptom of the disease appears." In order that active immunization may be produced by preventive inoculation, the antigen should contain the essential immunizing fraction in sufficient concentration, the dose should be ample and exposure should not occur before complete protection has developed. There is no test for the presence of the

10. Doull, J.; Shibley, G., and McClelland, J.: Active Immunization Against Whooping Cough, Am. J. Pub. Health **26**:1097, 1936.

11. Schick, B.: Immunity, Allergy and Anaphylaxis, in Brennemann, J.: Practice of Pediatrics, Hagerstown, W. F. Prior, Company, Inc., 1937, vol. 1, p. 6.

immunizing fraction. The relationship between a positive agglutinin test or a positive complement fixation test and immunity has not been proved. Topley and Wilson [12] said:

> The ultimate court of reference in determining the efficacy of active immunization must be the observation of the behaviour of immunized persons when exposed to the risk of natural infection.

Mishulow, Mowry and Orange [7] questioned the possible sensitization to therapeutic serums which may be used subsequently through the injection of vaccine grown on horse or sheep blood. They found that 1 cc. of toxin vaccine contained 0.00041 cc. of sheep serum. Kahn,[13] however, said:

> When vaccines are prepared of microorganisms requiring blood, it is well to avoid the use of horse serum. Traces of horse serum proteins in vaccine may be sufficient to exert a slight immunizing effect on the child who becomes latently immune to horse serum and the injection of horse serum in later years may activate this latent immunity and cause relatively marked responses to these injections.

## CONCLUSIONS

Inoculation with potent antigen confers protection on a high percentage of young children. Occasional failures doubtless occur in spite of flawless technic in the preparation, the preservation and the administration of the vaccine because there are no tests for the standardization of antigen in regard to its essential immunizing fraction. Humoral phenomena, such as agglutinin response and complement fixation reactions, are not criteria of tissue immunity. Exposure to the disease is the ultimate test of immunity.

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12. Topley, W., and Wilson, G.: The Principles of Bacteriology and Immunity, London, Edward Arnold & Co., 1936, p. 1096.

13. Kahn, R.: Tissue Immunity, Springfield, Ill., Charles C. Thomas, Publisher, 1936, p. 629.

# ACUTE ANTERIOR POLIOMYELITIS IN NEW YORK IN 1935

## A REVIEW OF SIX HUNDRED AND EIGHTY-SIX CASES

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The purpose of this paper is to present some new and important aspects of poliomyelitis as seen in the epidemic that was prevalent in the city of New York in 1935. This was the third largest outbreak in New York during the past twenty-five years. The largest number of cases, 9,023, was recorded in 1916; 4,138 cases were reported in 1931 and 2,054 in 1935.

These observations were made at the Willard Parker Hospital, to which 686 of the 2,054 patients in the 1935 epidemic were admitted. Most of the patients came from Manhattan and the Bronx. The incidence of the disease was 27 per hundred thousand in these boroughs. Since Leake and his co-workers [1] expressed the belief that 10 cases of the paralytic form per hundred thousand a year is the normal or average rate for a given community, the 1935 outbreak, therefore, was of moderate epidemic proportions.

### SEASON

About the middle of July 1935 a more than seasonal prevalence of poliomyelitis was noted. Thereafter, the reported cases increased daily until the last week in August, when the epidemic reached its peak. A general decline began in September and continued through October (chart 1). The entire seasonal curve corresponded almost exactly to that of the previous outbreaks in this locality.

### AGE

Although poliomyelitis is primarily a disease of children, it occurs also in adolescents and in adults. In the recent epidemics there has been

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1. Leake, J. P.; Cedar, E. T.; Dearing, W. P.; Gilliam, A. G., and Chope, H. D.: Epidemiology of Poliomyelitis in California, 1934, Am. J. Pub. Health **24**:1204 (Dec.) 1934.

a greater tendency for it to affect the older age groups (table 1). During the 1916 epidemic in New York only 1.7 per cent of the cases occurred in persons over 15. In 1931 the figure had risen to 4.9 per cent, while in 1935, 13 per cent of the patients were 15 or over. Likewise, in the California and the Denmark outbreak of 1934, a larger number of older patients were affected than had been previously, more than 32 per cent of the patients being more than 14.[2]

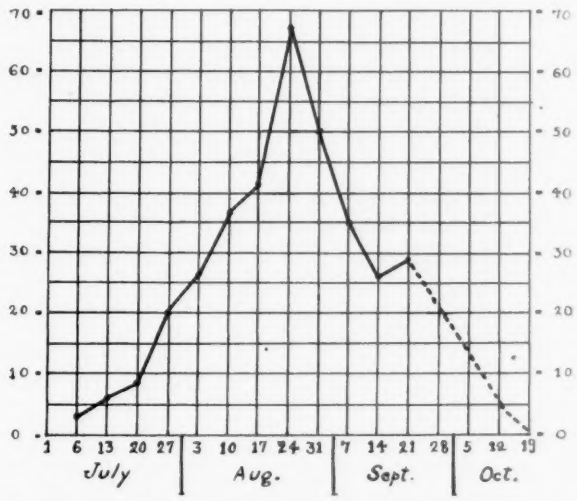


Chart 1.—Cases of poliomyelitis in New York city from July 1 to Oct. 1, 1935: weekly occurrence by date of onset. (From the *City of New York, Department of Health, Quarterly Bulletin* for Nov. 1, 1935.)

TABLE 1.—*Age Incidence in Various Outbreaks (Percentage)*

| | Year | Total No. of Patients | Under 1 Year | 1-4 Years | 5-9 Years | 10-14 Years | 15-19 Years | 20 and Over |
|---|---|---|---|---|---|---|---|---|
| New York City*..... | 1916 | 9,023 | 11.1 | 66.8 | 15.8 | 2.5 | 0.8 | 0.9 |
| | 1931 | 4,138 | 4.2 | 48.1 | 31.4 | 10.4 | 3.0 | 1.9 |
| | 1935 | 2,054 | 1.8 | 31.8 | 41.6 | 15.6 | 5.4 | 3.8 |
| Denmark..... | 1934 | 3,938 | 1.0 | 19.0 | 24.0 | 22.0 | 16.0 | 18.0† |
| California..... | 1934 | 2,648 to August 18 | 17.0 | | 27.0 | 24.0 | 12.0 | 20.0† |

* Figures obtained through Dr. Samuel Frant, of the New York city department of health.
† Approximate percentage, calculated from the number of cases.

In the 1935 outbreak in New York 33.6 per cent of the patients were under 5 years, and 75 per cent were under 10. Twelve patients were under 1 year, the youngest patient being 2½ months old. The

2. Jensen, C.: The 1934 Epidemic of Poliomyelitis in Denmark: Preliminary Report on the Epidemiology, Clinical Features and Convalescent Serum Therapy, Proc. Roy. Soc. Med. **28**:1007 (June) 1935. Leake.[1]

oldest patient was 48. The age distribution in the 686 cases at the Willard Parker Hospital (table 2) corresponded closely to that in the 2,054 cases reported in the entire city.

### SEX AND COLOR

Of the 686 patients, 413, or 60 per cent, were males and 273, or 40 per cent were females. The preponderance of males was therefore similar to that which was found in nearly all past epidemics. The statement that Negroes are not as susceptible to poliomyelitis as white people was not borne out in this epidemic,[3] as 6 per cent of the cases occurred in Negroes (8 per cent of the population of Manhattan and the Bronx is Negro).

### COMMUNICABILITY (MULTIPLE CASES) AND INCUBATION PERIOD

More than 1 case of poliomyelitis occurred in 17 of 667 families, an incidence of 2.5 per cent. In these 17 households there were at least 36 definite cases. The rate of secondary cases generally varies from 2 per cent to 6 per cent in an epidemic. Two exceptions are noteworthy, the California epidemic of 1934, in which multiple cases occurred in 12 per cent of the families, and the Quebec epidemic of 1932, in which more than 1 case of poliomyelitis occurred in 13 per cent of the families.[4] If one were to include the mild illnesses[5] which not infrequently arise coincidentally with definite attacks of poliomyelitis, the degree of communicability in the 1935 epidemic was considerably greater than 2.5 per cent. We were unable, however, to investigate thoroughly all the mild illnesses which were reported to us, many of which may have been abortive poliomyelitis. A single family may be cited to illustrate the coincidental occurrence of these

TABLE 2.—*Age Incidence at the Willard Parker Hospital*

| Age, Years | Number of Cases | Percentage |
|---|---|---|
| Under 5 | 231 | 33.7 |
| 5-9 | 270 | 39.3 |
| 10-14 | 96 | 14.0 |
| 15-19 | 59 | 8.5 |
| Over 20 | 30 | 4.5 |
| | 686 | 100.0 |

3. Harmon, P. H.: The Racial Incidence of Poliomyelitis in the United States with Special Reference to the Negro, J. Infect. Dis. **58**:331 (May-June) 1936.

4. Foley, A. R.: The 1932 Epidemic of Poliomyelitis in Quebec, Canad. Pub. Health J. **25**:260 (June) 1934.

5. Paul, J. F.; Salinger, R., and Trask, J. D.: "Abortive" Poliomyelitis, J. A. M. A. **98**:2262 (June 25) 1932.

mild illnesses. In this family 6 of the 7 children were taken ill within a short time of one another with symptoms suggestive of poliomyelitis. A lumbar puncture was performed on 4, and definite pleocytosis was found in each case.

In 14 of the 17 households with multiple cases the clinical form of the poliomyelitis was similar. In 9 of these the siblings had the nonparalytic type, while in 5 the afflicted children had the paralytic form. In only 3 was the form of the disease in the secondary cases different from that in the primary one.

It is highly significant that none of the hospital personnel exposed to the disease contracted it. This is in marked contrast to the findings in the Los Angeles epidemic of 1934, in which over 15 per cent of the employees of the division of contagious diseases of the Los Angeles County Hospital contracted poliomyelitis.[6]

The first detectable symptoms in the secondary cases appeared within one week of those in the primary case in all but 3 families (table 3). In 6 families symptoms in the secondary cases developed within one

TABLE 3.—*Interval Between the Onset of Symptoms in Multiple Cases*

| Days | 1 | 3 | 4 | 5 | 6 | 7 | 9 | 13 | 31 |
|---|---|---|---|---|---|---|---|---|---|
| Cases | 6 | 2 | 1 | 3 | 3 | 1 | 1 | 1 | 1 |

day of those in the primary case. The longest interval between a primary and a secondary case was thirty-one days. This occurred in one family; a nonparalytic type of poliomyelitis appeared in a brother ten days after the first patient returned home from the hospital. In spite of the long interval which had elapsed, an effort was made to isolate the virus from the nose of the first patient. The nose was irrigated with sterile water thirty-six days after the onset of the illness. The washings were filtered and concentrated. A search for the virus, however, was unsuccessful, and the monkey into whom the concentrated nasal washings were injected intracerebrally did not acquire poliomyelitis. The failure to isolate the virus from the nasal secretions,[7] a task rather difficult and frequently unsuccessful, did not exclude the probability that we were dealing with a carrier. The other possibility, of course, was that the second patient had been infected with the poliomyelitic virus from another source.

6. Kessel, J. F.; Hoyt, A. S., and Fisk, R. T.: Use of Serum and the Routine and Experimental Laboratory Findings in the 1934 Poliomyelitis Epidemic, Am. J. Pub. Health **24**:1215 (Dec.) 1934.

7. Flexner, S., and Amoss, H. L.: Persistence of the Virus of Poliomyelitis in the Nasopharynx, J. Exper. Med. **29**:379 (April) 1919.

### RECURRENCE OF THE DISEASE

Second attacks of poliomyelitis are rare. Quigley [8] reviewed the literature to 1934 and collected 11 cases, adding 1 case of his own, in which the outcome was fatal. In our series there was a 7 year old boy who had been stricken with poliomyelitis previously, in 1933. During his first attack paralysis of the peronei muscles of the right lower extremity took place. In the second attack further paralysis in the right leg and thigh and weakness in the left thigh and the abdominal muscles occurred. The clinical features of this case and the results of a study of the neutralizing properties of the serum are being reported separately.[9]

### CLASSIFICATION

We have classified poliomyelitis into four main types: (1) nonparalytic, (2) spinal paralytic, (3) bulbar and (4) encephalitic.

1. Nonparalytic type: There were fever, vomiting, pain in the back of the neck or in the spine and other symptoms suggestive of meningeal irritation. Only those cases were included in which the spinal fluid contained at least 20 cells per cubic millimeter.

2. Spinal paralytic type: There was decided weakness or paralysis of the muscles supplied by segments of the spinal cord.

3. Bulbar type: There was involvement of the structures in the medulla oblongata and the pons as manifested by facial weakness, nasal voice, dysphagia, dysarthria or respiratory distress of central origin.

4. Encephalitic type: The patient was drowsy, delirious, comatose or convulsive or had diplopia.

Thirty-nine patients displayed clinical evidence of involvement of more than one division of the central nervous system, e. g., bulbospinal involvement. As was pointed out by Landon and Smith,[10] the pathologic changes observed at autopsy are not limited necessarily to the areas which were obviously affected during life.

The incidence of the different types is shown in table 4.

It is important to bear in mind that of the total number of patients observed, 282 entered the hospital without signs of paralysis. Of these, 225 passed through the entire clinical course without having muscular weakness, and only 57 had paralysis.

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8. Quigley, T. B.: Second Attacks of Poliomyelitis: Review of the Literature and Report of a Case, J. A. M. A. **102**:752 (March 10) 1934.

9. Fischer, A. E., and Stillerman, M.: To be published.

10. Landon, J. F., and Smith, L. W.: Poliomyelitis, New York, The Macmillan Company, 1934.

PARALYSIS

Paralysis was present in all 12 infants less than 1 year old and in 51 of the 52 who were less than 2 years old (table 5). The high incidence of paralysis in children under 2 years of age may be due to the absence of protective antibody in young children or may be only relative, for the nonparalytic types are difficult to detect in persons of that age group. Early symptoms may be overlooked in young children. The incidence of various types of poliomyelitis by age groups is shown in table 5.

Although it is not shown in the table, only 1 of the 7 patients over 30 escaped paralysis. It is interesting that the number of patients

TABLE 4.—*Incidence of Types*

| Type | Number of Cases | Percentage |
|---|---|---|
| Nonparalytic | 225 | 33 |
| Spinal paralytic | 392 | 57 |
| Bulbar | 55 | 8 |
| Encephalitic | 14 | 2 |

TABLE 5.—*Incidence of Types According to Age*

| | Age, Years | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Under 5 | | | | | | | |
| Type | Under 1 | 1-2 | 3-4 | 5-9 | 10-14 | 15-19 | Over 20 | Total |
| Nonparalytic | 0 | 1 | 38 | 100 | 50 | 26 | 10 | 225 |
| Paralytic | 11 | 39 | 129 | 138 | 33 | 24 | 18 | 392 |
| Bulbar | 1 | 0 | 10 | 25 | 9 | 8 | 2 | 55 |
| Encephalitic | 0 | 0 | 2 | 7 | 4 | 1 | 0 | 14 |
| Number of cases | 12 | 40 | 179 | 270 | 96 | 59 | 30 | 686 |
| | | | 231 | | | | | |

having paralysis during the early part of the outbreak was 77 per cent, in comparison with 50 per cent in the latter half of the same epidemic. This may have been due either to a decrease in the virulence of the virus or, more likely, to the fact that the nonparalytic forms were more frequently recognized as physicians became aware of the existence of an epidemic.

Observations on the neutralizing capacity of serums from paralytic and nonparalytic patients were made.[11] These studies, however, did not offer any explanation for the varying incidence of paralysis in the different age groups.

11. Brodie, M.; Fischer, A. E., and Stillerman, M.: Neutralization Tests in Poliomyelitis: Sera Taken During the Acute and Convalescent Stages of the Disease and Tested with a Passage Virus and a Strain Isolated During the 1935 New York City Outbreak, J. Clin. Investigation **16**:447 (May) 1937.

MORTALITY

The mortality from poliomyelitis varies within wide limits and in a particular age group is in proportion to the number of cases of paralysis. Table 6 shows that the case fatality expressed in percentages in both 1931 and 1935 was highest for infants and for persons over 20, the age groups in which the percentage of paralysis was greatest.

It has been observed that the mortality rate for poliomyelitis has been declining in recent years. In the New York epidemic of 1916, when the nonparalytic form was not well known and there was paralysis in nearly all reported cases, the case fatality was 26.9 per cent. During 1931, 83 per cent of the patients treated in city hospitals (2,402) had paralysis and the mortality was 12.2 per cent, while in the 4,138 cases

TABLE 6.—*Case Fatality According to Age, Percentages*

| | Under 1 Year | 1-4 Years | 5-9 Years | 10-19 Years | Over 20 | Total |
|---|---|---|---|---|---|---|
| 1935 (Willard Parker Hospital) | | | | | | |
| Cases | 12 | 219 | 270 | 155 | 30 | 686 |
| Deaths | 2 | 3 | 2 | 7 | 4 | 18 |
| Percentage | 16.6 | 1.3 | 0.7 | 3.9 | 13.3 | 2.6 |
| 1931 (whole city) | | | | | | |
| Cases | 165 | 1,925 | 1,205 | 516 | 107 | 4,138* |
| Deaths | 32 | 201 | 146 | 92 | 33 | 504 |
| Percentage | 19.3 | 10.4 | 12.1 | 17.8 | 32.5 | 12.2 |

* Age of 220 patients not recorded.

TABLE 7.—*Duration of Illness in Which the Outcome Was Fatal*

| | Day After Onset on Which Death Occurred | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 3d | 4th | 5th | 6th | 7th | 8th | 9th | 11th | 12th | 20th |
| Number of cases | 1 | 2 | 3 | 3 | 2 | 1 | 2 | 2 | 1 | 1 |

reported for the entire city the percentage of paralysis was 69.9 per cent. In the 1935 outbreak, 65 per cent of the patients seen at the Willard Parker Hospital had paralysis. The mortality rate for the hospital was only 2.6 per cent, while that for the entire city was 4.5 per cent. This is the lowest mortality rate that the city of New York has ever experienced. The rate in the Los Angeles epidemic of 1934 (1.5 per cent) was even lower, although about 50 per cent of the patients were paralyzed.

Of the 18 patients that died in the acute stage in this series, 12 were males and 6 females. Two of these were Negro. Death occurred within the first week of illness in the majority of cases. The duration of the illness in the cases in which the outcome was fatal is shown in table 7. It is significant that only 1 of the 282 patients that entered the hospital without paralysis died.

### PATHOLOGY

All the patients who died showed signs of bulbar involvement during their illness. Careful postmortem studies were made of 5. The essential pathologic process was acute nonsuppurative inflammation of the central nervous system. The spinal cord and the medulla oblongata showed various degrees of perivascular infiltration (cuffing), degeneration of the nerve cells with neuronophagia, edema, congestion, petechial hemorrhages and gliosis. Of these conditions, the most frequent were the perivascular cuffing and the degeneration of the nerve cells. The changes were most prominent in the motor cells of the anterior horns of the spinal cord. The alterations in the gray and white matter of the cerebrum and the cerebellum were slight and infrequent. The meninges often showed lymphocytic infiltration, more so over areas of the brain and the spinal cord in which distinct lesions were noted. Anatomic changes were frequently found in other organs also. Toxic hepatitis was noted in 4 of the 5 cases and in 3 there was toxic splenitis. The thymus was large in all cases. The lungs showed varying degrees of congestion, edema, emphysema and atelectasis. In 1 case small areas of lobular pneumonia, probably hypostatic, were present. This patient and one other who died were in the respirator for seventeen and forty-two hours, respectively. The pulmonary changes in these two patients were essentially the same as those in the patients who had not been placed in the apparatus.

### SYMPTOMATOLOGY

It has been stated frequently that the symptomatology of poliomyelitis varies from year to year. This statement was to some extent substantiated in 1935. The earliest clinical symptoms—fever, headache, nausea and vomiting—were mainly those of some general constitutional disturbance. These symptoms, which ushered in the clinical picture, were either symptoms of a systemic infection which subsequently localized in the central nervous system or toxic manifestations of a primary disease of the central nervous system. The prevalent opinion favors the latter point of view.[12] In the epidemic under discussion, the onset of these symptoms was most frequently sudden and without definite signs of involvement of the brain or the spinal cord. The development of meningeal signs—pain and stiffness of the back of the neck and the spine—usually appeared from twenty-four to

12. Fairbrother, R. W., and Hurst, E. W.: The Pathogenesis of and Propagation of the Virus in Experimental Poliomyelitis, J. Path. & Bact. **33**:17, 1930. Faber, H. K.: Acute Poliomyelitis as a Primary Disease of the Central Nervous System, Medicine **12**:83 (May) 1933. Brodie, M., and Elvidge, A. R.: The Portal of Entry and Transmission of the Virus of Poliomyelitis, Science **79**:235 (March 9) 1934.

seventy-two hours after the onset. In a small number of cases the meningeal signs appeared after the early symptoms had subsided and the patient had felt well for several days. On the other hand, the course was occasionally so rapid and progressive that paralysis appeared within twenty-four hours. The most significant early sign of involvement of the central nervous system was pain and stiffness of the back of the neck and the spine which was accentuated on flexion of the neck. To overcome this discomfort, patients on getting into the sitting position would often first turn to one side, push themselves upright and maintain this position by propping themselves up with their hands behind them for support.

Transient drowsiness and vertigo were the symptoms commonly observed. The throat was often slightly injected, but other symptoms of involvement of the upper part of the respiratory tract were infrequent. Constipation was the rule, while diarrhea was uncommon. Abdominal pain, usually in the region of the umbilicus, was present in some patients for the first few days, and it was sometimes accompanied by retention of the urine. Pain in the extremities and over the trunk sometimes preceded the appearance of paresis or paralysis. It was not uncommon for pain to persist for a number of days either in the nonparalytic stage or after the development of paralysis. Sometimes there were paresthesias and tenderness in the paralyzed areas. Twitchings of the face and the extremities were sometimes noted in the more severely ill patients. Generalized glandular involvement was not found.

The superficial and the deep reflexes in the nonparalytic stage were usually within normal limits or slightly increased. When flaccid paralysis developed, the tendon reflex, of course, disappeared. The Kernig and the Brudzinski sign were often positive with nuchal or spinal rigidity. Occasionally a diagnostic lumbar puncture was followed by a positive Kernig or Brudzinski sign which persisted for the following day or two. One could make no prediction by the reflex changes in the nonparalytic stage whether paralysis might develop. However, the reappearance of reflexes in the paralyzed parts usually coincided with the return of function. The shorter the interval between the onset of paralysis and the return of reflexes, the more complete and more rapid was the recovery.

Urinary retention was present in some cases early in the disease. Usually it was transient and lasted from one to four days. However, in 1 case it lasted ten days and in another at least twenty-one days.[13] With few exceptions, urinary retention occurred only in patients who were paralyzed or had signs of encephalitis.

13. We were unable to communicate with this patient after she left the hospital.

In the cases in which there was bulbar involvement the most common symptoms were difficulty in swallowing, accumulation of mucus in the throat, nasal voice, nasal regurgitation of fluids, facial weakness and dysarthria. The dysphagia usually disappeared in from one to twelve days when the patient survived. However, facial weakness and the nasal twang often persisted for one year or more. The dysarthria was usually associated with dysphagia and regurgitation of fluids through the nose. In several cases diplopia, blurred vision and pain in the eyes were noted. The fundi were normal in such cases. Ophthalmoplegia was observed in 3 cases. Convulsions were noted in only 3 cases and

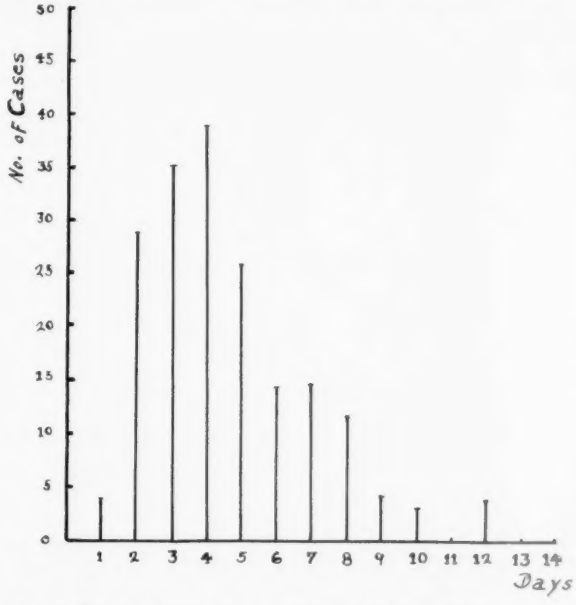


Chart 2.—Duration of fever in the nonparalytic patients. The patients who were without fever on admission to the hospital were omitted from the tabulation.

aphonia in one; deafness or disturbance of the vestibular mechanism were not observed. There were no permanent changes in the sensorium.

At the onset the temperature usually ranged from 100 to 103 F. Occasionally it reached 104 or 105 F. The duration of the fever was of much greater significance than its height. We have illustrated the duration of the fever both in the nonparalytic patients (chart 2) and in the paralytic patients (chart 3). In 80 per cent of the nonparalytic patients the temperature fell to normal in five days, while 60 per cent of the paralytic patients had fever for more than five days. Consequently, if the fever lasts more than five days in a nonparalytic patient, one should look for the probable development of paralysis. Occasionally, prolonged fever (lasting from ten to twelve days) was observed. This

usually denoted the presence of some complication, not necessarily related to poliomyelitis. The duration of the fever in patients with bulbar involvement corresponded to that in the paralyzed patients. The patients who died had terminal hyperpyrexia.

Of the 282 patients admitted to the hospital in the nonparalytic stage, 57, or 20 per cent, subsequently became paralyzed. Chart 4 illustrates the day of illness on which paralysis was first noted. In about four fifths of the cases it developed in the first week of illness. When paralysis appeared before the fifth day, a temperature of from 100 to 103 F. was present. However, no definite relationship was

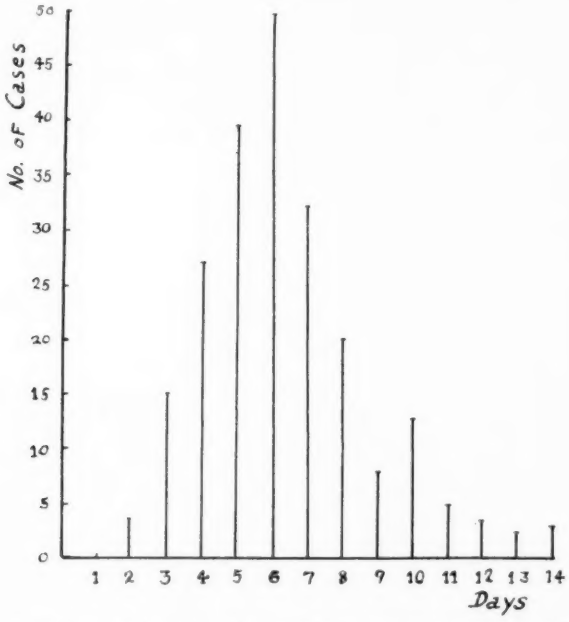


Chart 3.—Duration of fever in the paralytic patients. The patients who had no fever and were paralyzed on admission to the hospital were omitted from the tabulation.

found between the height of the temperature and the onset of paralysis. In about half of the patients the fever had subsided when paralysis was first observed. This was due to the fact that the onset of paralysis was sometimes so gradual that it was not apparent for some days after the acute infection appeared to subside. Consequently, when a patient has completed the sixth or seventh day of his disease and does not have paralysis, he will probably recover completely.

Spontaneous functional recovery occurred in most cases. This often began as early as the first week after the appearance of the paralysis. The degree of improvement was often marked. On the other hand,

some patients with extensive involvement showed almost no perceptible change in their physical status for months after the onset of the disease.

When the disease progressed and terminated fatally during the acute stage of the illness, a fairly common picture was observed. The temperature usually rose sharply to from 104 to 107 F. or remained at a high level; the respirations became rapid, shallow, jerky and irregular; cyanosis appeared and did not respond to oxygen; the extremities became cold, and profuse perspiration of the skin occurred. The patient was unable to take fluids by mouth and vomited frequently. Extreme drowsiness or coma set in, and twitching or convulsions were often

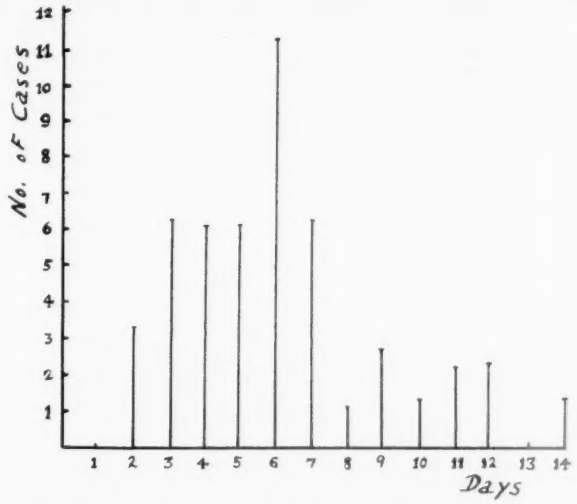


Chart 4.—The day of illness on which the paralysis was first noticed in non-paralytic patients who acquired paralysis subsequent to hospitalization.

noted. The pulse was usually rapid and of good quality until just before death, which generally was due to respiratory failure.

### SPINAL FLUID

A lumbar puncture was performed at the time of admission to the hospital in all cases in which poliomyelitis was suspected unless one had been made previously. The fluid was examined cytologically immediately after withdrawal. Blood-tinged fluid was discarded. The fluid, as is usual in poliomyelitis, was clear or hazy and under slightly increased pressure. The albumin and the globulin content were increased. The sugar content was within normal limits. There were from 0 to 1,080 cells per cubic millimeter, with mononuclear cells predominating. No correlation could be drawn between the type of cellular reaction and the severity of the illness.

Careful tabulations of the cytologic picture in relation to the day of the lumbar puncture were made. It was found that in the majority of cases of nonparalytic, bulbar or encephalitic poliomyelitis the cell count ranged between 50 and 200 cells per cubic millimeter while in most cases of the paralytic form it varied from 0 to 100 cells. Since the patients with paralysis usually entered the hospital later in the course of their illness, the puncture was performed on most of them on the fourth or fifth day after the onset, while the puncture was performed on most of the nonparalytic or encephalitic patients on the second or third day. The height of the count, therefore, was to some extent dependent on the day of the illness on which the lumbar puncture was performed. The number of cells in the spinal fluid fell gradually with the decline of the acute stage of the illness. After the ninth day the count was less than 50 cells per cubic millimeter in practically all cases. There were a few cases of spinal paralytic or bulbar involvement in which there was no pleocytosis although the fluid was removed during the first week. Levinson [14] recorded similar observations. The pleocytosis was significant only when there were over 500 cells per cubic millimeter. Such pleocytosis was present in 12 cases in this series, and in 8 of these paralysis had recently occurred or developed shortly thereafter.

Thus it appears that the degree of pleocytosis varied with the day of the illness and did not have any prognostic value unless the count was over 500 cells per cubic millimeter. The cell count did not serve to differentiate one type of poliomyelitis from another.

A pellicle frequently formed in the spinal fluid. This occurred in fluids having a low count as well as in those having a high count. The pellicle did not aid in differentiating poliomyelitis from other diseases, for it occurs in the spinal fluid in all cases of tuberculous meningitis, in some cases of encephalitis [15] and in cases of aseptic meningitis.[16]

### DIFFERENTIAL DIAGNOSIS

Patients admitted to the hospital for poliomyelitis and subsequently proved to have another condition may be subdivided into three groups. In the first group were those that had symptoms of a general systemic disease such as grip, without localized signs. Those who had a disease which produced stiffness of the neck or signs suggesting invasion of the brain and meninges were in the second group. The diseases represented included meningitis, pneumonia with meningismus, epidemic

14. Levinson, S. O.: Early Acute Anterior Poliomyelitis Without Increase of Cells in the Spinal Fluid, J. Pediat. **1**:337 (Sept.) 1932.

15. Neal, J.: Personal communication to the authors.

16. Viets, H. R., and Watts, J. W.: Acute Aseptic Meningitis, J. Nerv. & Ment. Dis. **83**:253 (Sept.) 1934.

and postvaccinal encephalitis, tetany, sinusitis, cervical adenitis, rheumatic fever involving the muscles of the neck and dysentery with cerebral symptoms. In the third group were patients with conditions simulating bulbar or paralytic poliomyelitis, such as Bell's palsy, conditions caused by cerebrovascular accidents, osteomyelitis, arthritis, epiphysitis and injuries to joints. Thus, it is seen that as in previous epidemics a large number of different diseases presented a clinical picture easily mistaken for some phase of poliomyelitis.

The question also arose during the epidemic as to whether the poliomyelitis, particularly the nonparalytic form, was not a disease due to another virus. In the past few years a new disease entity, benign lymphocytic choriomeningitis, or acute aseptic meningitis, caused by a specific filtrable virus has been described by Armstrong and Lillie [17] and by Rivers and Scott.[18] Earlier cases in which the clinical picture was similar were recorded by Wallgren [19] and by Viets and Watts.[20] The symptoms of this disease are similar to those of nonparalytic poliomyelitis, and differentiation of the two diseases clinically is practically impossible. Certain facts, however, have led us to the opinion that the nonparalytic patients we studied did not have choriomeningitis. Nearly all the reported cases of this disease in which the diagnosis was confirmed by serologic study have occurred in adults. The spinal fluid usually contained between 500 and 2,000 lymphocytes per cubic millimeter, and this count persisted for several weeks. Weakness and paralysis occurred infrequently in choriomeningitis, whereas 20 per cent of the nonparalytic patients in this epidemic had some paralysis during their period of hospitalization. Most important was the failure of the blood serum from convalescent patients to protect mice against the virus of acute aseptic choriomeningitis.

The possibility of encephalitis similar to that which occurred in St. Louis in 1933 was also considered. There, much older age groups were attacked; only 13 per cent of the patients were less than 16 years old. In that outbreak disorientation, mental confusion and blurred vision were the common symptoms, while paralysis was infrequent. The blood serum of nonparalytic convalescent patients in the New

17. Armstrong, C., and Lillie, R. D.: Experimental Lymphocytic Choriomeningitis of Monkeys and Mice Produced by a Virus Encountered in Studies of the 1933 St. Louis Encephalitis Epidemic, Pub. Health Rep. **49**:1019 (Aug. 31) 1934.

18. Rivers, T. M., and Scott, T. F. M.: Meningitis in Man Caused by a Filterable Virus: Identification of the Etiological Agent, J. Exper. Med. **63**:415 (March) 1936.

19. Wallgren, A.: Une nouvelle maladie infectieuse du système nerveux central (Meningite aseptique aiguë), Acta pædiat. **4**:158, 1925.

20. Viets, H. R., and Watts, J. W.: Aseptic (Lymphocytic) Meningitis, J. A. M. A. **93**:1553 (Nov. 16) 1929.

York epidemic also failed to neutralize the 1933 St. Louis encephalitis virus when injected intracerebrally into mice [21] according to the method of Muckenfuss, Armstrong and McCordock.[22] Were one to assume that some of the cases of poliomyelitis without paralysis were cases of benign lymphocytic choriomeningitis or encephalitis, one would also have to assume that more than one nervous disease occurred in epidemic proportions at the same time.

During the New York epidemic of 1935 the poliomyelitis virus was isolated by Kramer and his co-workers [22a] from the nasal secretions of 2 paralytic patients and by Stillerman and Brodie [22b] from 1 patient with involvement of the medulla oblongata. This is important, since there is always extreme technical difficulty in demonstrating the presence of the virus.

### ONSET FOLLOWING TONSILLECTOMY AND ADENOIDECTOMY

Aycock and Luther [23] in 1929 and Silverman [24] in 1931 reported observations on the onset of poliomyelitis following tonsillectomy and adenoidectomy. Aycock and Luther reported 16 such cases, of which 11 were of the bulbar form. In all the cases in which tonsillectomy and adenoidectomy had been performed within one month of the onset of poliomyelitis, the operation had taken place between seven and eighteen days prior to the onset. Silverman reported 5 cases in which poliomyelitis followed such an operation; the disease in all was of the bulbar type and developed in from nine to nineteen days after the operation.

In our series 10 cases were found in which the operation had been performed within one month of the onset of poliomyelitis. In 5 of the 10 cases, bulbar and encephalitic manifestations occurred. This incidence was proportionately much greater than the 10 per cent incidence of the bulbar and the encephalitic forms throughout the epidemic (table 4). Closer study fixed the date of onset in 8 of the 10 cases at the

21. Brodie, M.: Neutralization Tests with the Aseptic Choriomeningitis and St. Louis Encephalitis Viruses: Convalescent Sera Obtained from Non-Paralytic Poliomyelitis Patients During the 1935 New York City Outbreak, to be published.

22. Muckenfuss, R. S.; Armstrong, C., and McCordock, H. A.: Encephalitis: Studies on Experimental Transmission, Pub. Health Rep. **48**:1341 (Nov. 3) 1933.

22a. Kramer, S. D.; Sobel, A. E.; Grossman, L. H., and Hoskwith, B.: Survival of the Virus of Poliomyelitis in the Oral and Nasal Secretion of Convalescents, J. Exper. Med. **64**:173 (Aug.) 1936.

22b. Stillerman, M., and Brodie, M.: The Isolation of Virus from Nasal Washings During Acute Poliomyelitis in New York City in 1935, to be published.

23. Aycock, W. L., and Luther, E. H.: The Occurrence of Poliomyelitis Following Tonsillectomy, New England J. Med. **200**:164, 1929.

24. Silverman, A. C.: Acute Poliomyelitis in Syracuse, N. Y., Am. J. Dis. Child. **41**:829 (April) 1931.

tenth, eleventh or twelfth day, in 1 at the sixteenth day and in 1 at the twenty-second day after the operation. The interval corresponded closely to the incubation period of experimental poliomyelitis in monkeys. It is recognized, of course, that a certain number of children ordinarily have their tonsils and adenoids removed during the summer months, and it is impossible to state whether these children would have contracted poliomyelitis had they not had this operation performed. However, the fairly uniform period between the operation and the onset of poliomyelitis in 8 of the 10 cases suggested that the poliomyelitis virus entered the system during or shortly after the operative procedure. In view of these findings, one should consider that a risk is incurred when this operation is performed during an epidemic of poliomyelitis. The details of these cases will be published separately.[25]

### POLIOMYELITIS IN PREGNANCY

One patient contracted poliomyelitis in her eighth month of pregnancy, with complete paralysis of the lower extremities and some weakness of the abdominal muscles. She came to term and spontaneously delivered a healthy infant, who showed no evidence of poliomyelitis. Similar cases in which the infant was unaffected by poliomyelitis are reported in the literature.[26]

### THE SCHICK TEST

The question of the susceptibility of children to both poliomyelitis and diphtheria has been widely discussed in the literature. Zingher[27] found that the reaction to the Schick test was more frequently positive in children with poliomyelitis than in well children or children with scarlet fever or measles in comparable age groups. His observations, however, were recorded before immunization against diphtheria was widespread. Aycock[28] has repeatedly stressed the epidemiological similarity between poliomyelitis and diphtheria in respect to age groups and the development of subclinical immunity. Foley[4] found an even more direct relationship in the 1932 epidemic. He stated that in the vicinity of Quebec the morbidity rate and the mortality rate for poliomyelitis were highest in the counties in which immunization against diphtheria had not been carried out and was lowest in those in which the population was largely protected against diphtheria. This apparent selectivity

25. Fischer, A. E., and Stillerman, M.: To be published.

26. Brahdy, M. B., and Lenarsky, M.: Acute Epidemic Poliomyelitis Complicating Pregnancy, J. A. M. A. **101**:195 (July 15) 1933.

27. Zingher, A.: The Schick Test in Poliomyelitis, Scarlet Fever, Measles and in Normal Children, Am. J. Dis. Child. **13**:247 (March) 1917.

28. Aycock, W. L.: Immunity in Virus Diseases, J. A. M. A. **97**:1199 (Oct. 24) 1931.

of the poliomyelitis virus for persons who had not been inoculated against diphtheria suggested to Foley the possibility that increased resistance to poliomyelitis was present in children who were immune to diphtheria. This idea was also expressed by Armstrong.[29] However, Harrison,[30] in a survey of 159 cases of poliomyelitis and a control group, was unable to detect any influence of previous immunization against diphtheria on the incidence of poliomyelitis, an apparent contradiction of Foley's deductions. Because of these different points of view, it was decided to study the relation of immunity against diphtheria to poliomyelitis in this epidemic. A Schick test and a control test were made on the patient's admission in every case of poliomyelitis, and an attempt was made to obtain a history of previous immunization. Of the 686 patients, 210 (31 per cent) had a positive reaction to the Schick test, and 85 (40 per cent) of these were children under 5 years of age. Of the 210 who had a positive reaction, 71 had previously been immunized against diphtheria and 21 of these were less than 5 years old; 63 had not been immunized, and in 76 the history of immunization was indefinite. It was surprising to see so many positive reactions in persons previously immunized. However, the significant feature of this analysis was not so much the frequency of a positive reaction to the Schick test as the intensity of the reaction. In many persons the site of infection became bullous. This reaction was so outstanding that in some patients who had mild symptoms of poliomyelitis it served as a diagnostic aid. The site of positive reactions to Dick tests done at the same time never became bullous.

The frequency of bullous reactions to the Schick test early in poliomyelitis was investigated further. Eight persons having this type of reaction were retested after the acute stage of the illness had subsided. In 6 the reaction was negative when the test was repeated. One who had reacted with the formation of a bleb gave a positive reaction without a bleb when retested, and in 1 the reaction was unchanged. None of these patients received diphtheria toxoid or antitoxin during the interval between the tests. The amount of diphtheria toxin in one Schick test is insufficient to produce the changed reaction.[31] The results of these tests raised the question as to whether the Schick test performed during the acute stage of poliomyelitis is a true index of susceptibility to diphtheria. Several possibilities are suggested:

1. Is one dealing with a temporary loss of immunity and an increased susceptibility to diphtheria?

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29. Armstrong, C.: Post Vaccinal Encephalitis, Pub. Health Rep. **47**:1553 (July 22) 1932.

30. Harrison, W. T., cited by Armstrong.[29]

31. Schick, B.: Personal communication to the authors.

2. Is altered reactivity of the skin present during the acute stage of poliomyelitis, and is it the cause of the bullous type of reaction?

3. Does the level of diphtheria antitoxin, which is normally present in the blood and tissues, change during the acute stage of poliomyelitis?

The Schick reaction in other acute infectious diseases was studied in detail by one of us.[32] Bullous reactions were not infrequently encountered in cases of pneumonia. This study suggested that the Schick reaction may be altered not only in poliomyelitis but early in the course of some of the other acute infectious diseases.

## TREATMENT

Absolute rest was the most important therapeutic measure employed. This was insured by keeping the patients flat in bed, using sedatives when necessary and placing boards beneath the mattress in cases in which there was severe spinal pain and rigidity.

When paralysis was first evident, the extremities were placed and held by sandbags in a position capable of giving the most relaxation to the affected muscles to prevent their overstretching. After the temperature had been normal for several days and all tenderness of the muscles had disappeared, plaster casts and splints were applied to maintain this position and to counteract possible contracture. After twenty-one days patients were sent to their homes or to an orthopedic hospital if they required further treatment.[33]

No convalescent human serum, whole blood or horse serum of any kind was administered to any patient in this series.

The patients with the bulbar form were treated actively. The most distressing symptoms were accumulation of saliva and mucus in the throat and nasal regurgitation due to involvement of the muscles of the pharynx and the soft palate. These patients were placed in the Trendelenburg position, and suction of the throat by means of a soft rubber catheter was employed. Those who were unable to swallow liquids had their intake of food maintained by means of gavage through a nasal catheter, hypodermoclyses and intravenous infusions. When the involvement was extensive and it appeared that intravenous injections would have to be resorted to repeatedly, the intravenous drip method was employed. When cyanosis occurred, oxygen was administered by nasal catheter or oxygen tent.

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32. Rubin, B., and Fischer, A. E.: To be published.

33. The Sanitary Code of the City of New York Department of Health has been modified so that patients with poliomyelitis may be released from quarantine after fourteen days.

TREATMENT BY MEANS OF THE RESPIRATOR

Eighteen patients required the use of the respirator. The indications for placing a patient in the respirator included dyspnea, tachypnea, use of the accessory muscles of respiration, abdominal breathing, inability to cough or to raise sputum, cyanosis, exhaustion, irritability and tachycardia. In 8 patients the respiratory distress was due entirely to weakness or paralysis of the muscles supplied by the thoracic or cervical segments of the spinal cord, e. g., the intercostal muscles or the diaphragm. These patients had the spinal type of the disease. In the other 10 patients signs of bulbar as well as of thoracic involvement were present; these patients had the bulbospinal type. No patients with the purely bulbar type were placed in the respirator. All the patients treated in the respirator also had extensive paralysis of the skeletal muscles in other parts of the body.

Six of the eight patients who had paralysis of the respiratory muscles due only to involvement of the spinal cord survived. The 2 deaths occurred seven and eighteen months, respectively, after the onset of the illness. They were caused by atelectasis and pneumonia. In contrast, 8 of the 10 patients with bulbospinal involvement died, 7 during the acute stage and one a year later. Pneumonia developed in 5, and 3 of these died. The eighth patient lived in the respirator for a year before succumbing to pneumonia. One of the patients with extensive paralysis of the thoracic muscles survived two attacks of pneumonia but succumbed to a third.

The management of patients in the respirator has been described by Wilson [34] and by Brahdy and Lenarsky.[35] However, in the light of previous experience, some changes were made in the treatment during this epidemic. The negative pressure exerted by the machine was not allowed to become excessive. The patients who showed respiratory difficulty were watched closely and were not permitted to become exhausted before being placed in the respirator. When the intercostal muscles recovered their power, the patient was at first allowed to be out of the respirator for a short time. The period was increased slowly, but even after the patient was able to remain out for twenty-four hours without any discomfort he was replaced daily for two hours for months. This helped to maintain the tone of the paralyzed muscles and was an aid in the prevention of deformities of the chest.[36]

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34. Wilson, J. L.: Respiratory Failure in Poliomyelitis: Treatment with the Drinker Respirator, Am. J. Dis. Child. **43**:1433 (June) 1932.

35. Brahdy, M. B., and Lenarsky, M.: Treatment of Respiratory Failure in Acute Epidemic Poliomyelitis, Am. J. Dis. Child. **46**:705 (Oct.) 1933.

36. Legg, A. T.: The Use of the Drinker Respirator in the After-Care of Infantile Paralysis, J. A. M. A. **100**:647 (March 4) 1933.

COMMENT

Nonparalytic forms of poliomyelitis were recognized more frequently than in previous outbreaks.

It is impossible to predict in which patients paralysis will develop. Patients with severe constitutional reactions during the first few days of their illness do not necessarily become paralyzed, although with the persistence of their symptoms the likelihood increases.

Many neutralization tests were carried out on serum from both nonparalytic and paralytic patients during the acute and the convalescent period of the disease.[11] It was hoped that a correlation might be demonstrated between the virus-neutralizing ability of the serum and the degree of immunity or of recovery. Early in the disease neutralizing substances were found in the serum of 18 of 32 nonparalytic patients and in only 14 of 82 paralytic patients. They were also found in the preparalytic stage in the serum of 2 of 4 patients who subsequently had paralysis. None of the nonparalytic and only a few of the paralytic patients without neutralizing or protective substances in the early stage of the disease had demonstrable antibodies in the serum within one year of the onset of the illness. In this study no evidence was found of a definite relation between the presence of protective substances in serum and (1) resistance to poliomyelitis, (2) the diagnosis of the nonparalytic form of poliomyelitis or (3) the degree of recovery from paralysis.

Shortly after the beginning of the 1935 outbreak it was evident that there were again large numbers of nonparalytic patients. In view of the experience gained in the 1931 outbreak,[37] it was decided not to use any serum or transfusions in this epidemic. In 1931 a control group of patients seen in the preparalytic, or what is better called the meningitic, stage of the disease, did not receive serum and did as well as those who received serum. In 1935, when no serum was given, only 20 per cent of the 282 patients that entered the hospital in the meningitic stage subsequently acquired paralysis, in comparison with 31 per cent of 477 patients who received convalescent serum in 1931. These figures offer further evidence that the spontaneous course of poliomyelitis can be favorable without any treatment other than rest in bed and routine care.

The prospect of surviving was much better for patients who entered the hospital without paralysis than for those who were paralyzed. In the 1935 outbreak only 1 of the 282 nonparalytic patients died (0.3 per cent), as compared with 17 of the 404 patients who were paralyzed

37. Fischer, A. E.: Human Convalescent Serum in the Treatment of Preparalytic Poliomyelitis: A Comparison of 477 Treated and 102 Control Patients in New York City in 1931, Am. J. Dis. Child. **48**:481 (Sept.) 1934.

when first seen (4.2 per cent). This observation confirms one which was made in 1931,[37] when the mortality for 579 patients seen in the meningitic stage of the disease was 3.4 per cent, in comparison with the high mortality, 12.2 per cent, for the entire epidemic. One can, therefore, state definitely that a patient showing only signs of meningeal irritation at the height of the illness offers a much better prognosis than one in whom paralysis is already present.

SUMMARY

An analysis of 686 cases of the poliomyelitis outbreak in the city of New York in 1935 was undertaken. The seasonal incidence and the distribution as to the age, sex and color of the patient were recorded. The tendency for the disease to attack older persons was greater than previously. The communicability was low; 36 cases occurred in 17, or 2.5 per cent, of the families. One case of recurrent poliomyelitis was found in this series. The proportion of patients paralyzed was highest in the very young, 51 of 53 children under 2 years being paralyzed, and in patients over 30, 6 of 7 being paralyzed. Paralysis developed in only 20 per cent of the patients that entered the hospital in the preparalytic or meningitic stage. The nonparalytic attacks were probably caused by the poliomyelitis virus, rather than by other viruses that attack the central nervous system. The temperature was the best criterion of the activity of the disease. In 8 of 12 cases in which the spinal fluid contained over 500 cells per cubic millimeter, paralysis either was present or developed shortly. In 10 cases poliomyelitis occurred within one month after a tonsillectomy and adenoidectomy, and in 5 of these there were bulbar or encephalitic manifestations. One case of poliomyelitis occurred in a patient who was in her eighth month of pregnancy. A strongly positive reaction to the Schick test was frequently found early in the disease. Treatment in the Drinker respirator of patients with respiratory embarrassment due to paralysis of the muscles of the chest or diaphragm was satisfactory. The mortality rate for the 686 cases, 2.6 per cent, was the lowest ever recorded in New York city.

Seventy-Three East Ninetieth Street.
Foot of East Fifteenth Street.

# BLOOD SUGAR IN DIABETES IN CHILDREN

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In the clinical management of diabetes mellitus, adequacy of control is best gaged by the degree of oscillation of the blood sugar level during twenty-four hours. Basing interpretations on single estimations of the blood sugar is almost as unsafe as depending on isolated urinalyses as a basis for assurance that satisfactory management is being maintained. The occurrence of nocturnal hyperglycemia is usual after the disease is well established, but the part that this endogenous elevation of the blood sugar level plays in the hyperglycemia and glycosuria of later hours is frequently overlooked. In some clinics it is customary to determine the level of the blood sugar under fasting conditions, after the administration of insulin but before the ingestion of food, and at various intervals after the ingestion of a meal. With such information and a constancy of regimen, a fair estimate can be formed as to the status of control of the diabetes.

Hoping to devise additional laboratory approaches to the control of diabetes, we conducted investigations of the changes in the blood sugar level of diabetic children. These investigations pertain to the nocturnal fluctuations of the blood sugar level, the course of the blood sugar level in the early morning hours after awakening but before the ingestion of food or the administration of insulin and the response to standardized doses of insulin unaccompanied by food.

While nocturnal hyperglycemia is usually not present at the onset of the disease, it tends to appear within a few months.[1] Subsequent to the rise and fall of the blood sugar level following the absorption of the evening meal, the level again rises during sleep, often reaching markedly hyperglycemic levels by the time of awakening. To permit adequate control of the diurnal hyperglycemia, nocturnal doses of

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From the Department of Pediatrics, State University of Iowa College of Medicine.

1. White, P.: Diabetes in Childhood and Adolescence, Philadelphia, Lea & Febiger, 1932, p. 77. Priesel, Richard, and Wagner, Richard: Die Zuckerkrankheit und ihre Behandlung im Kindesalter, Leipzig, Georg Thieme, 1932.

insulin are frequently required, especially with the child. In the brief study pertaining to this phenomenon herein reported, successive determinations of the blood sugar level were made, 11 diabetic subjects being used. The first determination was made about 9:30 p. m., a second sample was obtained at midnight or subsequently and a third was obtained in the early morning. In some instances additional samples were drawn during the interim. The data obtained are offered in table 1. In every subject the blood sugar level of the morning exceeded that of the preceding night; the net increase varied from 40 to 115 mg. In most instances an abnormally hyperglycemic level had been reached. The rise of the blood sugar level did not follow a constant velocity; in some instances the peak occurred before the terminal sample was drawn.

TABLE 1.—*Nocturnal Blood Sugar Values of Diabetic Children (Expressed as Milligrams per Hundred Cubic Centimeters)*

| Subject | P.M. | | | | A.M. | | | | | Rise |
|---|---|---|---|---|---|---|---|---|---|---|
| | 9:30 | 10 | 11 | 12 | 1:30 | 3 | 4 | 5 | 6 | |
| M. A. | 220 | ... | ... | ... | 250 | ... | ... | 300 | ... | 80 |
| C. S. | 175 | ... | ... | ... | 195 | ... | ... | 215 | ... | 40 |
| R. A. | ... | 155 | ... | 240 | ... | 220 | ... | ... | 145 | 85 |
| T. A. | ... | 125 | ... | 135 | ... | 185 | ... | ... | 180 | 60 |
| D. H. | 90 | Insulin | ... | ... | 90 | ... | ... | 180 | ... | 90 |
| K. C. | 90 | ... | Insulin | ... | 65 | ... | ... | 145 | ... | 55 |
| T. A. | 65 | ... | Insulin | ... | 70 | ... | ... | 125 | ... | 60 |
| M. M. | 55 | Insulin | ... | ... | 50 | ... | ... | 125 | ... | 70 |
| V. F. | ... | Insulin | 75 | ... | ... | ... | 130 | 175 | 190 | 115 |
| H. B. | ... | Insulin | 50 | ... | ... | ... | 115 | 120 | 135 | 85 |
| G. J. | ... | 45 | ... | Insulin | ... | ... | ... | ... | 145 | 100 |

Is this rise of the blood sugar level during the fasting state dependent on sleep and inactivity? The data obtained in the second phase of this study show that it is not. Estimations of the blood sugar were made at 7 and 7:30 a. m. for 24 diabetic children who had not received insulin for several hours previously and who had had no food since the preceding night. Without exception the second value was higher than the first, the difference ranging from 10 to 155 mg., with an average elevation of 35 mg. Although the initial blood sugar levels ranged from 45 to 550 mg., no apparent relationship existed between the degree of elevation and the initial value. The data pertaining to this study are offered in table 2.

Neither nocturnal hyperglycemia nor diurnal elevation of the blood sugar level during fasting is noted in the nondiabetic person, and he does react to the administration of insulin. Is his response comparable to that noted in the diabetic patient? As a means of investigating this problem, a series of insulin tolerance tests were made in which the

response of diabetic and that of nondiabetic children were compared. A total of 299 separate tests were completed, 207 with diabetic and 92 with nondiabetic subjects. One hundred children with diabetes were studied and their responses compared with those of 90 nondiabetic children who were free from discernible chronic infection, latent syphilis or neurosyphilis excepted, and from apparent endocrine disturbance. The nondiabetic children had been receiving the routine hospital diet, which is sufficiently stable to standardize the influence of diet on the sensitivity to insulin. The diabetic children were free from evidence of acidosis; they had been receiving similar standardized diets, with the ratio of fatty acid to dextrose maintained at 1 : 1½ for all ages. The allowance of protein, minerals, vitamins and calories was

TABLE 2.—*The Blood Sugar Values During Fasting of Diabetic Children at 7 and 7:30 A. M. (Expressed as Milligrams per Hundred Cubic Centimeters)*

| Blood Sugar Levels During Fasting | | | Blood Sugar Levels During Fasting | | |
|---|---|---|---|---|---|
| 7 A.M. | 7:30 A.M. | Rise | 7 A.M. | 7:30 A.M. | Rise |
| 45 | 65 | 20 | 230 | 290 | 60 |
| 65 | 75 | 10 | 255 | 295 | 40 |
| 65 | 90 | 25 | 260 | 300 | 40 |
| 80 | 110 | 30 | 285 | 315 | 30 |
| 95 | 110 | 15 | 320 | 340 | 20 |
| 105 | 115 | 10 | 320 | 365 | 45 |
| 120 | 160 | 40 | 325 | 350 | 25 |
| 165 | 185 | 20 | 350 | 440 | 90 |
| 170 | 215 | 45 | 375 | 405 | 30 |
| 175 | 190 | 15 | 470 | 625 | 155 |
| 185 | 200 | 15 | 480 | 555 | 75 |
| 205 | 265 | 60 | 550 | 580 | 30 |

designed to meet fully the requirements for normal growth and activity.

The dose of insulin for each child, whether diabetic or nondiabetic, was one-fourth unit per kilogram of body weight. It was administered in the morning with the patient fasting, all injections being made subcutaneously in the intrascapular region, so as to minimize the variability in the rate of absorption. Blood for analysis was obtained from the fingertip immediately before the administration of insulin and at half-hour intervals thereafter for two hours. Determinations of the dextrose were made, on 0.2 cc. of blood, the Somogyi method for the precipitation of protein and a modification of the Folin-Wu method for the development of color being employed.

As would be expected, the blood sugar level of the nondiabetic subjects fell abruptly to hypoglycemic levels. The level reached was maintained with little variation for the two hour period of observation; an almost negligible tendency toward elevation was noted at the final

determination. The response of the diabetic subjects differed in several respects from that of the normal subjects. For the first half hour the fall in the blood sugar level was gradual, and then, without exception, further lowering was observed, with acceleration of the rate of fall. A direct relation was noted between the initial level of the blood sugar and the extent of the depression observable during the first half hour. In all instances the greatest rate of fall was found during the second and the third half-hour period; during the last half hour the rate of depression was retarded, and in the diabetic children whose initial values lay between 50 and 70 mg. the blood sugar level tended to climb during the terminal half hour.

For statistical purposes, various correlations of the data have been made. One group of correlations deals with the response throughout the two hour period of observation, whereas another pertains to a comparison of the records of the half-hour responses.

The absolute degree of the two hour response of the blood sugar to the insulin was measured by two indexes, the net milligram drop and the average milligram drop. The former represents the difference between the initial blood sugar level and the final blood sugar level; the latter, the difference between the initial level and the average of the four subsequent determinations. In addition, the relative degree of response was calculated, by dividing the net milligram drop by the initial blood sugar value.

In dealing with the half-hour intervals, corresponding correlations were made. The half-hour relative velocity was obtained by dividing the difference between the blood sugar levels of any two half-hour intervals by the first of the two values.

Table 3 gives a summary of the data, together with the three correlations for the two hour periods, the net, the average and the relative milligram drop in the blood sugar level. A striking proportionality is to be noted between the net or the average milligram drop and the initial value for the blood sugar. The relative reduction of the blood sugar level in the group with initially normal blood sugar levels (both normal and diabetic subjects) is similar throughout the limited range of the initial values. The corresponding values for the diabetic subjects whose initial blood sugar values were 120 mg. per hundred cubic centimeters or higher are considerably greater than those for the normoglycemic group. With the blood sugar level not exceeding 300 mg., the standard dose of insulin (one-fourth unit per kilogram) was enough to restore the normal glycemic level within two hours; with the initial level exceeding 300 mg., the terminal value two hours after the administration of insulin was hyperglycemic, the hyperglycemic level being

proportional to the magnitude of the initial level. However, the amount of sugar disappearing from the blood stream in a two hour period was proportional to the initial level of the blood sugar; the greater the sugar content, the greater the apparent efficiency of the insulin. In the normoglycemic zone, no distinction is apparent between the diabetic and the nondiabetic subjects as to the total effect of insulin. Berg and his co-workers,[2] studying depancreatized dogs, noted the same apparently increased efficacy of insulin during hyperglycemia but pointed out that when the amount of sugar removed in a given period is considered

TABLE 3.—*Insulin Tolerance Tests: Average Blood Sugar Values at Half-Hour Intervals (Expressed as Milligrams per Hundred Cubic Centimeters) and Average Deviations (Measured by the Three Indexes, Net Milligram Drop, Average Milligram Drop and Relative or Percentage Drop)*

| Range of Initial Value | Before Insulin | After Insulin | | | | Net Mg. Drop After 2 Hr. | Average Mg. Drop During 2 Hr. | Percentage Drop After 2 Hr. | Number of Tests |
|---|---|---|---|---|---|---|---|---|---|
| | | ½ Hr. | 1 Hr. | 1½ Hr. | 2 Hr. | | | | |
| **Nondiabetic Subjects** | | | | | | | | | |
| 60- 79 | 76 | 55 | 51 | 51 | 50 | 26 | 24 | 34.2 | 27 |
| 80- 99 | 87 | 64 | 55 | 55 | 56 | 31 | 29 | 35.6 | 49 |
| 100-119 | 108 | 76 | 71 | 63 | 65 | 43 | 39 | 39.8 | 16 |
| **Diabetic Subjects** | | | | | | | | | |
| 60- 79 | 70 | 61 | 50 | 47 | 52 | 18 | 14 | 25.7 | 4 |
| 80- 99 | 85 | 78 | 55 | 54 | 54 | 31 | 27 | 36.5 | 8 |
| 100-119 | 110 | 98 | 67 | 55 | 55 | 55 | 40 | 50.0 | 9 |
| 120-149 | 138 | 121 | 88 | 61 | 54 | 84 | 57 | 60.8 | 14 |
| 150-199 | 171 | 157 | 116 | 77 | 64 | 107 | 67 | 62.7 | 21 |
| 200-249 | 222 | 214 | 174 | 129 | 97 | 125 | 68 | 56.4 | 34 |
| 250-299 | 270 | 254 | 206 | 157 | 118 | 152 | 86 | 56.3 | 37 |
| 300-349 | 320 | 298 | 236 | 178 | 129 | 191 | 110 | 59.6 | 33 |
| 350-399 | 374 | 359 | 277 | 219 | 168 | 206 | 98 | 55.2 | 20 |
| 400-449 | 417 | 378 | 312 | 226 | 178 | 239 | 144 | 57.3 | 15 |
| 450-499 | 468 | 446 | 353 | 286 | 219 | 249 | 142 | 53.3 | 7 |
| 500-549 | 543 | 492 | 405 | 297 | 235 | 299 | 177 | 56.0 | 5 |

in relation to the total amount of sugar present, proportional amounts are removed in the unit of time at all levels of glycemia. Since in this regard diabetic and nondiabetic persons react similarly within the zone of normal glycemia, the relative efficacy of insulin is not demonstrably different for the two types.

A study of the changes noted at half-hour intervals shows a distinction between the diabetic and the nondiabetic subjects at all levels of glycemia (tables 4 and 5). The response of the nondiabetic organism to insulin is prompt and rapidly reaches its maximum. In the diabetic

2. Berg, B. N.; Gross, J.; McJafee, J., and Zucker, T. F.: Blood Sugar Curves in Normal and Diabetic Dogs After Intravenous Injection of Insulin, Proc. Soc. Exper. Biol. & Med. **32**:1080, 1935.

subject, on the other hand, much latency of response is apparent, the fall during the second half hour exceeding that of the first and the effect continuing to manifest itself throughout the two hours of observation

TABLE 4.—*The Deviations of the Blood Sugar Concentrations at Half-Hour Intervals Following the Administration of Insulin to the Fasting Subject (Expressed as Milligrams per Hundred Cubic Centimeters, the Initial Value Being Used as a Standard of Comparison)*

| Range of Initial Value | Blood Sugar Deviations at | | | |
|---|---|---|---|---|
| | ½ Hour | 1 Hour | 1½ Hours | 2 Hours |
| | | Nondiabetic Subjects | | |
| 60- 79 | —21 | — 4 | 0 | — 1 |
| 80- 99 | —23 | — 9 | 0 | + 1 |
| 100-119 | —32 | — 5 | — 8 | + 2 |
| | | Diabetic Subjects | | |
| 60- 79 | — 9 | —11 | — 3 | + 3 |
| 80- 99 | — 7 | —23 | — 1 | 0 |
| 100-119 | —12 | —31 | —12 | 0 |
| 120-149 | —17 | —33 | —27 | — 7 |
| 150-199 | —14 | —41 | —39 | —13 |
| 200-249 | — 8 | —40 | —45 | —32 |
| 250-299 | —16 | —48 | —59 | —39 |
| 300-349 | —22 | —62 | —58 | —49 |
| 350-399 | —15 | —82 | —58 | —51 |
| 400-449 | —39 | —66 | —86 | —38 |
| 450-499 | —22 | —93 | —67 | —63 |
| 500-549 | —42 | —87 | —108 | —62 |

TABLE 5.—*The Relative Changes of the Blood Sugar Levels at Half-Hour Intervals Following the Administration of Insulin to the Fasting Subject (Expressed as Percentage of the Blood Sugar Value Observed at the Beginning of the Half-Hour Interval)*

| Range of Initial Value | The Relative Blood Sugar Changes at | | | |
|---|---|---|---|---|
| | ½ Hour | 1 Hour | 1½ Hours | 2 Hours |
| | | Nondiabetic | | |
| 60- 79 | —28.0 | — 7.5 | 0.0 | 0.0 |
| 80- 99 | —25.9 | —14.0 | 0.0 | + 1.9 |
| 100-119 | —29.6 | — 9.2 | —10.4 | + 3.1 |
| | | Diabetic | | |
| 60- 79 | —12.8 | —18.1 | — 6.0 | + 6.4 |
| 80- 99 | — 8.2 | —29.3 | — 2.2 | 0.0 |
| 100-119 | —10.9 | —30.0 | —17.9 | 0.0 |
| 120-149 | —12.3 | —27.7 | —30.9 | —11.4 |
| 150-199 | — 8.2 | —26.4 | —33.8 | —17.0 |
| 200-249 | — 3.6 | —18.7 | —25.9 | —24.9 |
| 250-299 | — 5.9 | —18.9 | —23 8 | —24.8 |
| 300-349 | — 6.9 | —20.8 | —24.5 | —27.5 |
| 350-399 | — 4.0 | —22.8 | —21.0 | —23.2 |
| 400-449 | — 9.4 | —17.5 | —27.6 | —21.2 |
| 450-499 | — 4.7 | —20.8 | —19.0 | —23.4 |
| 500-549 | — 7.9 | —17.7 | —26.6 | —20.9 |

and probably longer. Direct proportionality is apparent between the initial level of the blood sugar and the degree and the duration of the response.

The studies herein reported confirm observations made by numerous other observers [3] that the velocity of reaction following the administration of insulin is different in the diabetic and the nondiabetic subject and that this does not depend on the initial level of the blood sugar. The reason for this difference is not evident. Observers who have used the intravenous route of administration have noted a more rapid recovery from the effect of insulin in each group of subjects, but it seems reasonable to suppose that this is due to some degree of excretion of insulin when it is given intravenously and prolonged absorption when it is given subcutaneously.

Practical applications of the results of the studies herein reported are suggested in the following paragraphs.

Nocturnal hyperglycemia occurs spontaneously in patients with diabetes, and this reflects itself in the response of the blood sugar to the morning meal. It is combated most effectively through the administration of a nocturnal dose of insulin. Evidence indicates that such a dose is more effective if it is given some time after midnight rather than at an earlier hour. The same tendency to hyperglycemia during fasting is present in the day as well; the patient who requires more than minimal amounts of insulin requires a basic amount of insulin even though food is withheld.

Since the blood sugar level of the diabetic subject reacts at a different tempo from that of the nondiabetic subject, an insulin tolerance test may prove as valuable a means of diagnosing the presence of diabetes as is the dextrose tolerance test. The work of some investigators suggests that the hyperglycemia of hyperthyroidism may be distinguished from that of diabetes in this manner. The test as performed consists of the administration of one-fourth unit of insulin per kilogram of body weight and the determination of the blood sugar level before and at four half-hour intervals subsequently. The maximum reduction in the nondiabetic subject is observed within the first half hour, whereas in the diabetic subject the fall is prolonged into the second or third half hour or longer. This peculiarity of response seems inherent in the diabetic organism and is not determined by the initial blood sugar level, nor is there evidence that the nature of the response is altered by treatment of the disease.

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3. Bodansky, A., and Simpson, S.: The Blood Sugar of Normal Human Subjects After the Intravenous Injection of Insulin, Quart. J. Exper. Physiol. **17**:57, 1927. Norgaard, A., and Thaysen, T. E. H.: Clinical Investigations into the Effect of Intravenous Injections of Insulin: I. The Blood Sugar Curve of Normal Individuals, Acta med. Scandinav. **72**:492, 1929. Thaysen, T. E. H.: III. The Blood Sugar Curve in Diabetics, ibid. **73**:408, 1930. Berg and others.[2]

# SYMPATHETIC INNERVATION OF THE EXTERNAL SPHINCTER OF THE HUMAN BLADDER

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CHICAGO

It has been generally accepted that the external sphincter of the human bladder is composed solely of striated muscle innervated exclusively by the somatic nervous system (the pudic nerve arising from the third and fourth sacral roots).[1]

Doubt is thrown on this belief by the experimental findings in the following case, in which there was opportunity to observe the physiologic effects of stimulation of the peripheral and central ends of the sectioned pelvic sympathetic nerves (the presacral nerve). In this patient, it was observed that stimulation of the peripheral end of the cut presacral nerve caused muscular contraction at the junction of the prostatic and the membranous portion of the urethra, and the conclusion seems justified that in some cases there is an external sphincter of the human bladder innervated by the sympathetic system. Although it may be true that the innervation of the bladder in this case was fundamentally abnormal, the opportunities to make such physiologic observations on a human being are of necessity so limited that the findings in the following case seem worthy of record.

## REPORT OF A CASE

W. J. M., 14 years of age, was first admitted to the University of Chicago Clinics on Sept. 27, 1932, having been referred by Dr. Martin D. Jones, of Oak Park, Ill. It was stated that the child was perfectly well until 1928, when he sustained a severe blow across the lower part of the back. Subsequently, he complained of pain in that region and was confined to bed for two days, and retention of urine developed. This retention of urine, with frequent dribbling, continued for the four years before admission and, although at first he had been able to pass

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Part of a paper presented by one of the authors (D. N. B.) at the meeting of the American Pediatric Society, June 12, 1936, at Bolton Landing, Lake George, N. Y.

1. Learmonth, J. R.: A Contribution to the Neurophysiology of the Urinary Bladder in Man, Brain **54**:147-176, 1931.

urine when his bladder was much distended, for the past year he had been unable to void at all except when in a warm bath. Severe constipation had developed at the same time as the difficulty in micturition, and movement of his bowel was obtained only by the use of enemas.

The family history and previous medical history of the patient were irrelevant.

Examination revealed an undernourished boy. The abdomen was large and protuberant because of the enormous distention of the bladder. Pressure over the bladder produced pain in the back in the region of the kidneys, and the patient said that a similar pain frequently appeared spontaneously when the bladder became distended. The respiratory and cardiovascular systems seemed normal. Neurologic examination revealed a tuft of coarse black hair just below the lumbosacral junction in the midline of the back and a palpable defect of the spines and posterior arches of the sacrum. The left buttock and the left calf were smaller than the right. There was diminution of the perception of pain in the third, fourth and fifth sacral dermatomes, greater on the left side. The ankle jerk was unobtainable, and fibrillary twitchings were seen in the musculature of the left calf. There was bilateral pes cavus, more marked on the left side.

Examination of the urine showed that it contained albumin and pus cells. Examination of the blood showed leukocytosis, the white cell count being 13,000; 4,220,000 erythrocytes, and 85 per cent hemoglobin. The Wassermann and Kahn tests of the blood were negative. Chemical analysis of the blood revealed 27.7 mg. of nonprotein nitrogen per hundred cubic centimeters.

Roentgenograms of the lumbosacral portion of the spine showed absence of the spinous processes and laminae of the entire sacrum and absence of the spinous process and malformation of the laminae of the fifth lumbar vertebra.

The diagnosis was spina bifida occulta with myelodysplasia.

*First Operation.*—On Oct. 6, 1932, the lumbosacral region was explored through a posterior midline incision. The laminae of the fourth and fifth lumbar vertebra were removed and the sacral canal exposed. This revealed a gross malformation, for the spinal cord reached to the level of the first sacral vertebra and there terminated in a dense mass of connective tissue and fat, which completely filled the sacral canal (fig. 1). A small portion of this mass was removed, but because of the danger of damage to the sacral roots nothing radical was attempted.

*Postoperative Course.*—For a short time after the operation the patient's control over the bowel and the bladder was slightly improved, but soon the original condition returned. On Nov. 15 a temperature of 102 F. developed, with pain in the region of the kidneys and vomiting. This condition soon disappeared, only to recur in a more severe form early in December, and the patient was readmitted to the clinics on Dec. 7.

Examination then revealed little change except for the presence of definite tenderness on palpation over both kidneys. As much as 1,000 cc. of urine could frequently be obtained by catheterization.

A cystoscopic examination was made, which revealed a distended coarsely trabeculated bladder and a much weakened, patent internal sphincter.

A cystogram (fig. 2) was made after the injection of 340 cc. of a 5 per cent solution of sodium iodide into the bladder. This showed a large trabeculated bladder, a widely open, incompetent internal sphincter and a distended prostatic urethra.

An intravenous pyelogram, made after the injection of 40 cc. of skiodan, disclosed gross hydronephrosis of the right kidney. The left kidney was not visualized, and its function, therefore, was judged to be greatly impaired.

The diagnosis was paralysis of the bladder due to malformation of the sacral segments of the spinal cord (myelodysplasia).

*Second Operation.*—On Dec. 20, 1932, with the patient under spinal anesthesia, a midline abdominal incision was made. The fibers of the presacral nerve were isolated at the level of the sacral promontory, ligated and cut.

During the first part of the operation, Dr. H. E. Haymond introduced a cystoscope just through the junction of the prostatic and the membranous portion of the urethra (i. e., just through the external sphincter) and observed this area while the nerve was stimulated. The open internal sphincter and the prostatic bed were plainly visible. At no time was the observer aware of what was done within the abdomen, and he merely reported his own observations.

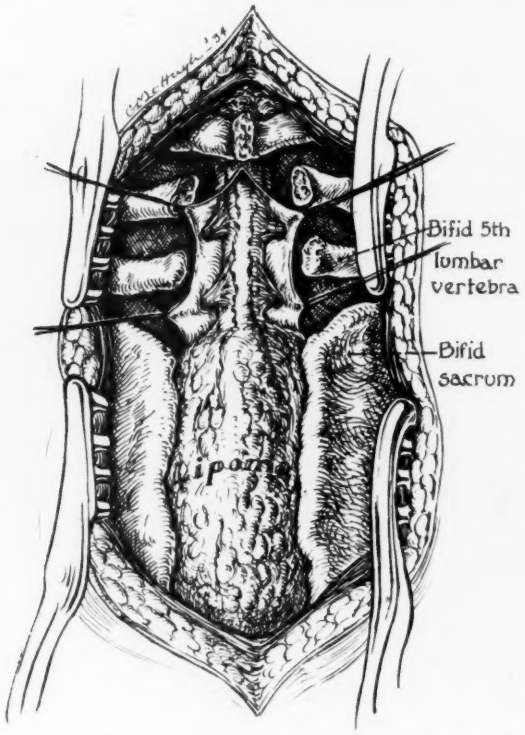


Fig. 1.—Drawing made from the operator's sketch, showing spina bifida of the sacrum and malformation of the spinal cord and cauda equina.

The peripheral end of the cut presacral nerve was stimulated on three occasions (10:50, 11 and 11:04 a. m.) with a faradic current just strong enough to elicit a contraction in the exposed rectus muscle. On each stimulation the fluid within the prostatic portion of the urethra immediately became clouded by the appearance of fluid from the prostatic bed. The cystoscopist stated that it seemed as if milk had suddenly been squirted into the field. This fluid contained spermatozoa. Coincident with the appearance of prostatic and seminal fluid the external sphincter suddenly tightened about the cystoscope so that it was practically impossible to move it. This contraction appeared with the beginning of stimulation, and the period of latency was short. It persisted as long as the stimulus was

applied and subsided slowly (three to five seconds?) after the stimulus was removed. At no time was any contraction of the internal sphincter seen, although this region was carefully observed. During the last stimulation (11:04 a. m.) the verumontanum was closely watched. Immediately after the stimulation it decreased to about one half of the size prior to stimulation. How long this reduction in size persisted was not recorded. No observations were made of the ureteral orifices, the wall of the bladder or the trigon. Stimulation of the central end of the cut nerve evoked no response, subjective or objective. However, as the height of the anesthesia was unfortunately not recorded, this observation is not significant.

Fig. 2.—Cystogram showing that the bladder is dilated and the wall trabeculated. The incompetence of the internal sphincter is clearly shown, the dilated prostatic urethra being continuous with the cavity of the bladder.

A segment of the peripheral end of the presacral nerve was then excised and the wound closed.

*Postoperative Course.*—An indwelling catheter was inserted after the operation and was left in place until Jan. 4, 1933. On that day the patient voided on three occasions, and only 45 cc. of residual urine was present immediately after urination. He continued to void several times a day, and although the amount of residual urine varied from day to day it never approached the preoperative level. The bowels functioned well after operation, the patient having a daily normal evacuation.

The patient was discharged from the hospital on Jan. 20, 1933. Since then he has been seen frequently in the urologic outpatient department. At the time of writing (1936) there is no longer any residual urine in the bladder after he voids. There is some impairment in the sensibility of the bladder, although at times the patient is aware of a sensation of fullness. The bowels function well, requiring only an occasional enema.

## COMMENT

This child's difficulty seems definitely attributable to malformation of the sacral portion of the spinal cord associated with spina bifida occulta. This portion of the spinal cord was not completely functionless, as skin sensibility was only partially impaired and not completely lost, muscular power was diminished but not absent and the left side was more involved than the right. To this impairment of the activity of the sacral portion of the spinal cord can be attributed a diminution in the sensation of fulness of the bladder and weakness of the detrusor muscle which must, in a large measure, have been responsible for the urinary difficulty. However, this cannot be the complete picture. The internal sphincter is known to have been greatly weakened, for it was constantly widely dilated and the prostatic urethra acted as a component of the bladder. The external sphincter, composed of striated muscle, is innervated by the third and fourth sacral segments of the spinal cord and must also have been weakened as a result of the malformation. If there were no other "sphincteric" structure at the lower end of the prostatic urethra, this patient would probably have suffered from simple incontinence rather than from the marked urinary retention and overflow incontinence which were present. That there is another "sphincteric" mechanism than the striated muscle, which forms the external sphincter and is innervated by the pudic nerve, was clearly demonstrated at the time of operation. Stimulation of the presacral nerve (sympathetic nerves) induced an immediate and pronounced contraction of some structure encircling the urethra at the junction of the prostatic and membranous portions (the level of the external sphincter). This case presents no evidence as to what that structure is. It is possible that the striated muscle of the classic external sphincter is innervated by both sympathetic and somatic nerves, but since innervation of striated muscle is contrary to the knowledge of the action of the sympathetic nervous system elsewhere in the body, it is unlikely that it exercises such a vicarious function here. Smooth muscle exists in this location [2] and may well form a "sympathetic" external sphincter

2. Cunningham, D. J.: Text-Book of Anatomy, ed. 5, edited by A. Robinson, New York, William Wood & Company, 1927. Piersol, G. A.: Human Anatomy, ed. 8, Philadelphia, J. B. Lippincott Company, 1923. Bailey, F. R.: Text-Book of Histology, edited by O. S. Strong and A. Elwyn, New York, William Wood & Company, 1925.

of the bladder. It is found as circular and longitudinal bundles throughout the prostatic urethra, within the stroma of the prostate and as a layer in the capsule of the prostate. It is probable that this "sympathetic" external sphincter may act as a substitute for the internal sphincter (also of smooth muscle and innervated by the sympathetic nerves) when that structure is weakened by constant pressure and dilatation. Certainly, it appears more likely that such a structure, innervated by the sympathetic nervous system, rather than the classic external sphincter, innervated by the somatic system, is responsible for the long periods of occlusion of the urethra and the absence of incontinence seen in such patients.

The observation that stimulation of the sympathetic nerves to the bladder reduces the size of the verumontanum is, we believe, original This reduction may be due to vasoconstriction within this vascular structure.

Section of the presacral nerve was originally undertaken to remove what Learmonth[3] described as the "brake" action of the sympathetic nerve on the detrusor muscle, i. e., the inhibition of contraction of the detrusor muscle. This and other cases, which it is anticipated will subsequently be reported, have led us to doubt that such inhibition of contraction of the detrusor muscle by the sympathetic nerves in man is of great significance, if it is present at all. It is our impression that the improvement which occurs in these cases is due largely, if not entirely, to relaxation of the sphincters innervated by the sympathetic nervous system, both the internal sphincter, which was already greatly weakened in the instance recorded here, and the "sympathetic" external sphincter, located at the junction of the prostatic and the membranous portion of the urethra.

## SUMMARY

The case of a boy of 14 with urinary retention, overflow incontinence and severe constipation due to malformation of the sacral portion of the spinal cord is reported.

Section of the presacral nerve greatly improved the function of both the bowel and the bladder, and this improvement was maintained for more than three years after the operation.

This improvement, we believe, was due largely to relaxation of the sphincters innervated by the sympathetic nervous system.

3. Learmonth, J. R.: Neurosurgery in the Treatment of Diseases of the Urinary Bladder: I. Anatomic and Surgical Considerations, J. Urol. **25**:531-549, 1931; II. Treatment of Vesical Pain, ibid. **26**:13-24, 1931; III. Treatment of Certain Types of Vesical Paralysis, ibid. **26**:229-232, 1931.

Observations made during operation revealed that stimulation of the peripheral end of the cut presacral nerve causes: (*a*) contraction of some "sphincteric" structure, probably smooth muscle of the prostatic urethra and the prostate at the junction of the prostatic and membranous portions of the urethra, which we have termed the "sympathetic external sphincter"; (*b*) diminution in the size of the verumontanum, possibly as a result of vasoconstriction, and (*c*) emission of prostatic and seminal fluid.

# A NEW TUBERCULIN PATCH TEST

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When one introduces a new tuberculin test, one must show that it is really new and, at the same time, useful. Essentially, there are three types of tuberculin tests: (1) the cutaneous test of von Pirquet, (2) the intracutaneous test of Mantoux and (3) the percutaneous test of Moro. Of these, the Mantoux test, with increasing doses, gives satisfactory results. Since the doses can be graduated, the necessary amount of tuberculin can be brought into contact with the reacting tissue. Whenever a question of differential diagnosis arises, the Mantoux test is indispensable. Since with a 0.01 mg. dose this test corresponds in sensitivity to the much simpler Pirquet test, one should always begin with the Pirquet test. If the result of that is negative, one should proceed with the Mantoux test, using 0.1 mg. and finally 1 mg. Such a procedure eliminates reactivation of an old tuberculous lesion or aggravation of an active tuberculous process.

The percutaneous test of Moro, modified by Hamburger and Ernst Wolf and imitated by others, has an advantage over the Pirquet test, which is, however, chiefly psychologic—it does not frighten the child. It consists merely of rubbing an ointment into the skin, a procedure which is painless and simple and nearly as accurate as the Pirquet test.

Some time ago Moro attempted a new procedure, a tuberculin plaster test, which was unsuccessful. Since 1930 one of us (V.), in Germany, has tried out a patch test in the following manner: A drop of tuberculin was placed on a strip of adhesive tape and allowed to dry in the air. This plaster was then placed on the skin over the sternum, which had previously been cleansed with ether. The results were satisfactory. Similar attempts were made and described by Lautier,[1] Kahara,[2]

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1. Lautier, R.: Compt. rend. Soc. de biol. **64**:5 and 91, 1908.
2. Kahara, Z.: Ztschr. f. Kinderh. **2**:747, 1912.

Blumenau,[3] Schmidt-Weigerer,[4] Habetin[5] and Grozin.[6] This method has its disadvantages: The wait for the tuberculin to dry in the air is time consuming, the plasters are difficult to preserve and when liquid tuberculin is used there is no way of grading the dose. Also, owing to pressure when the plaster is applied, the drop is uncontrollably spread over the skin and appears at the edges of the plaster, causing irregular and often unpleasant and extensive reactions. Grozin[6] attempted to prevent this by pressing the plaster on the skin only at its edges.

Malmberg and Fromm[7] also described a plaster test. They made a mixture of tuberculin and the adhesive mass of the tape and used this mixture to make plasters 1 cm. square. Without being able to judge this plaster test from personal experience, we see two theoretical objections to it. First, such a plaster does not permit easy differentiation between the specific tuberculin reaction and a possible nonspecific reaction from the adhesive tape itself. Second, it does not allow a sufficient concentration of tuberculin, since if one increases the concentration of tuberculin in the adhesive mass, this increased amount cannot act because the adhesive quality of the plaster is diminished.

The purpose of this paper is to describe a new patch test, which has the advantage over all other tuberculin tests of simplicity. Thin filter paper is saturated with tuberculin, suspended in the air in a dust-free room and allowed to dry. This saturated filter paper when dry can be kept indefinitely. The paper is cut into 0.8 cm. squares and placed on adhesive tape with forceps. Three types of plasters are prepared in this way: (1) plasters equipped with old tuberculin alone, (2) plasters containing old tuberculin and bouillon control and (3) plasters containing old tuberculin, control material and bovine tuberculin. The distance between these squares must be at least 1 cm. When more than one square is used, each square is indicated by letter on the back of the plaster. For example: "T" indicates old tuberculin; "B," bovine tuberculin, and "C," control material. The adhesive side of the plaster can be protected with stiff gauze, like that in emergency adhesive bandages, which is removed just before use (fig. 1).

The tuberculin contained within the filter paper square is dry and therefore in its most concentrated form. By the natural moisture of the skin (perspiration insensibilis), this tuberculin is liquefied suffi-

3. Blumenau, N.: Ztschr. f. Tuberk. **22**:157, 1914.

4. Schmidt-Weigerer: Med. Klin. **9**:375, 1913.

5. Habetin, P.: Wien. klin. Wchnschr. **41**:703, 1928.

6. Grozin, Maurice: The Tuberculin Patch Test, Am. J. Dis. Child. **46**:17 (July) 1933.

7. Malmberg, N., and Fromm, B.: New Tuberculin Test, Acta pædiat. **10**: 435, 1931.

ciently to cause a cutaneous reaction. In spite of this dilution by moisture, the tuberculin remains sufficiently concentrated to cause a reliable cutaneous reaction.

The control square does not cause an inflammatory reaction. However, a sensitive skin may occasionally give a nonspecific irritative reaction due to the adhesive plaster. Therefore, it is better always to use a control square.

In the case of the bovine tuberculin squares, we were unable to obtain a true bovine tuberculin that would allow a diagnostic differentiation from the human type by means of tuberculin tests. Using the tuberculin which we received from the United States Department of Agriculture, we found that a person who reacts to bovine tuberculin usually reacts to human tuberculin and vice versa. Since the hygienic measures used by the milk industry in the United States are so effective, it is of hardly any practical value to try to differentiate the two types. Therefore, the "bovine" square can easily be dispensed with.

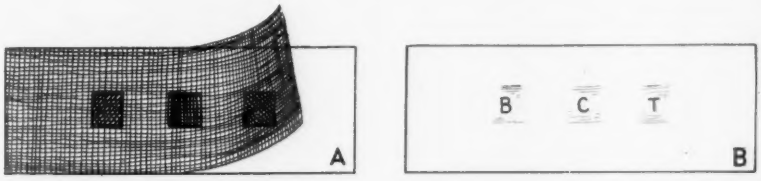


Fig. 1.—Diagram of the plaster used, *A* showing the adhesive side, covered by stiff gauze, and *B*, the outside, with letters to indicate the different squares.

In carrying out our tuberculin patch test we cleansed the skin with ether or benzene and then placed the plaster, from which the gauze had been removed, securely on the skin. After twenty-four hours the reaction was read, but the results were more reliable when the plaster was left on for forty-eight hours. The plaster may be removed with or without benzene. The reaction may be read immediately after removal or twenty-four hours later, at which time possible nonspecific skin reactions have disappeared and, on the other hand, the tuberculin reaction is intensified. In private practice one can instruct the mother or the nurse to remove the plaster after forty-eight hours and have the child brought to the office for reading of the results after seventy-two hours. The child must not be given a bath for the first two days, except perhaps a sponge bath during which care is exercised to keep the plaster dry.

When positive, the reaction appears as a sharply defined, indurated, reddened square, with lichenoid, follicular elevations on the skin (fig. 2). To secure clearcut reactions, we found it best to put the plaster

lengthwise on the sternum or transversely over the upper edge of the trapezius muscle and thus eliminate spreading of the tuberculin due to folds in the skin.

To prevent nonspecific cutaneous reactions it is necessary, as far as possible, to use an adhesive plaster that in itself will not cause irritation of the skin. However, even with persons with sensitive skin, in whom the plaster causes erythema, the interpretation of the tuberculin test is not difficult, because when the reaction is negative the tuberculin-covered area appears as a blanched square and when it is positive this area is more intensely red than the surrounding skin, in which a nonspecific reaction has taken place.

The simplicity of the test thus described is evident. It saves time by eliminating the preparation of different dilutions of tuberculin and their

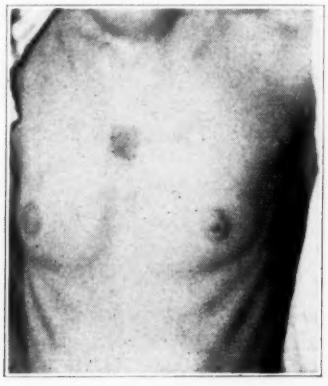

Fig. 2.—Photograph showing a positive reaction.

intradermal injection. It prevents the bruising of the skin by the Pirquet needle and also the wait of from five to ten minutes while the tuberculin dries. It is simpler and less time-consuming than the Moro test, which necessitates a hundred strokes for rubbing in the ointment and thorough scrubbing of the hands before and after the procedure. Most of all, it saves the child from pain and other unpleasant sensations, including the fear caused by visible preparations and manipulations with instruments (e. g., the syringe and the Pirquet needle). The tuberculin patch test takes but a moment to do and therefore is particularly practical when a large number of children are being tested, for instance, in schools or other institutions.

The reliability of this test can be seen in the table.

Of 209 tuberculous children, 187, or 89.5 per cent, showed a conformity between the results of the Pirquet test and those of our patch

test. The 22, or 10.5 per cent, in whom the results did not correspond consisted of 15 children, or 7.2 per cent, that showed a negative reaction to the Pirquet test and a positive reaction to the patch test and 7 children, or 3.3 per cent, that showed a positive reaction to the Pirquet test and a negative reaction to the patch test. When one considers these figures alone, the patch test described appears to be superior to the Pirquet test. However, in the 15 cases in which the results were unsatisfactory with the Pirquet test, these results may have been due to technical error.

Similarly, we do not wish to imply superiority of the patch test in the 2 cases in which the reaction to the Mantoux test was negative. In them, too, the possibility of a technical error may be considered, for example, in making up the dilutions for the Mantoux test.

The fact remains that our tuberculin patch test shows a distinct superiority over all other forms of patch test, and its results a more

*Data Illustrating the Reliability of the New Patch Test*

| Total Number of Cases: 209 | Cases | Percentage |
|---|---|---|
| Conformity between the Pirquet and the patch test | 187 | 89.5 |
| No conformity between the Pirquet and the patch test | 22 | 10.5 |
| Positive reaction to the patch test and negative reaction to the Pirquet test | 15 | 7.2 |
| Negative reaction to the patch test and positive reaction to the Pirquet test | 7 | 3.3 |

In 2 cases, positive reaction to the Mantoux test and negative reaction to the patch test.
In 2 cases, negative reaction to the Mantoux test and positive reaction to the patch test.

marked agreement with those of the Pirquet test. These favorable results may be due not only to the prolonged contact of the tuberculin with the skin (forty-eight hours) but also to the type of our patients. For the most part these patients were children with active tuberculosis, whose skin was highly sensitive to tuberculin.

The fundamental principle of our tuberculin patch test with saturated filter paper proved, after modification, to be fit also for an allergy patch test. This will be the subject of a future publication.

## SUMMARY

A new tuberculin patch test is described. The patch consists of a strip of adhesive tape on which a square of filter paper saturated with tuberculin has been placed.

Of 209 tuberculous children, 187, or 89.5 per cent, showed conformity between the results of the patch test and those of the Pirquet test. Of the 22, or 10.5 per cent, in whom the results did not conform, 15 were children who showed a positive reaction to the patch test and a negative reaction to the Pirquet test.

The patch test is not only as accurate, numerically, as the Pirquet test but shows the following definite advantages over all tuberculin tests:

1. It is painless and does not excite nervous children, and a good relation between the doctor and the patient is thus retained.

2. It consumes less time.

3. It does not involve the use of instruments and their sterilization or trauma to the skin through injection, scarification or rubbing.

4. It can be carried out without help or by a nurse or an assistant.

5. In contrast to all other patch tests, it creates a sharply limited area of reaction and prevents an uncontrollable spread of tuberculin on the skin.

6. It eliminates the danger of infection.

7. It has never led to a local or general constitutional reaction.

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# MINERAL COMPOSITION OF THE BONE AND CARTILAGE OF THE HUMAN FETUS

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The chemical study on bone and cartilage to be reported here supplements the work described in an earlier paper [1] on the mineral composition of the human fetus. In other investigations [2] made on similar material only a few of the mineral constituents have been considered. Apparently the percentage of some minerals remains fairly constant during short periods of fetal growth, but it has not been shown that this constancy persists for the entire fetal period or that the concentrations of other mineral elements show the same tendency. This investigation presents the values for the most important mineral constituents of specimens of bone and cartilage taken from twenty-one fetuses weighing from 197 to 4,150 Gm.

The material for this study was obtained at autopsy from eight to sixteen hours after death. Postmortem changes during the interval between death and autopsy were controlled as far as possible by refrigeration. The specimens of bone were stripped of soft tissue, and the cartilage was freed at the epiphysis and dissected clean. The bones, including the trabeculae and the marrow, were weighed immediately, dried at 105 C. to a constant weight, pulverized and then ashed in a platinum dish in a muffle furnace at 450 C. At the latter temperature a gray-white ash results, in which the minerals occur in the form of carbonates. The ash must be heated to a dull red heat in order that the carbonates may be converted to the corresponding oxides. Subjecting the ash to the higher temperature results in a loss of weight of about 6 per cent. In the process of ashing bone, the average amount of phosphorus lost is 2.6 per cent of the total phosphorus. The preparation of cartilage for chemical analysis is similar to that of bone, but a pure white ash is obtained at 450 C. The total fat content of both the bone and the cartilage was obtained by extracting the powdered substance for eight hours with alcohol and for sixteen hours with ether. The lipid phosphorus was then determined on the dried residue from the extract.

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1. Iob, V., and Swanson, W. W.: Mineral Growth of the Human Fetus, Am. J. Dis. Child. **47**:302 (Feb.) 1934.

2. (*a*) Toverud, K. U., and Toverud, G.: Acta pædiat. **16**:459, 1933. (*b*) Booher, L. E., and Hansmann, G. H.: J. Biol. Chem. **94**:195, 1931. (*c*) Logan, M. A.: ibid. **110**:375, 1935.

Standard chemical methods were used to determine the calcium,[3] magnesium,[4] sodium,[5] potassium [6] and phosphorus [7] in the solutions of the ash of bone and cartilage. In the case of bone, the potassium was determined on the filtrate after the removal of the calcium, magnesium and phosphorus by the method of Shohl and Bennett.[8] Determinations of the chloride,[2c] sulfur [9] and nitrogen by the Kjeldahl method were made directly on the pulverized dried bone and cartilage. Determinations of the carbon dioxide content of the limited quantities of material were not practicable and accordingly were not attempted.

## RESULTS AND COMMENT

Table 1 presents the physical constants and the water and the ash contents of the femurs and the tibias of twenty fetuses. The data show

TABLE 1.—*The Water and the Ash Content of the Fetal Femur and Tibia*

| | | Femur | | | Tibia | | |
|---|---|---|---|---|---|---|---|
| Fetus, No. | Weight, Gm. | Length, Cm. | Water, Percentage | Ash, Percentage | Length, Cm. | Water, Percentage | Ash, Percentage |
| 20 | 197 | ... | 46.3 | 60.2 | ... | .... | .... |
| 11 | 650 | 4.5 | 52.4 | 54.7 | 4.0 | 51.1 | 54.7 |
| 16 | 660 | 4.0 | 46.4 | 60.5 | 3.7 | 45.1 | 59.3 |
| 7 | 680 | 4.4 | 45.3 | 57.1 | 4.0 | 46.1 | 57.1 |
| 13 | 760 | 4.5 | 45.6 | 59.0 | 4.0 | 43.9 | 59.4 |
| 19 | 786 | ... | 48.2 | 63.4 | ... | .... | .... |
| 18 | 800 | 4.9 | 48.8 | 58.5 | 4.4 | 47.1 | 58.7 |
| 4 | 810 | 4.7 | 47.1 | 51.4 | 4.2 | 48.2 | 52.2 |
| 10 | 920 | 5.0 | 46.1 | 53.8 | 4.4 | 43.9 | 53.5 |
| 8 | 1,230 | 5.4 | 42.7 | 55.0 | 4.7 | 43.3 | 55.0 |
| 5 | 1,300 | 5.3 | 46.9 | 56.1 | 4.9 | 47.7 | 56.1 |
| 21 | 1,310 | 5.7 | 41.9 | 59.5 | 5.0 | 41.7 | 59.0 |
| 22 | 1,680 | 6.0 | 41.9 | 60.1 | 5.3 | 41.6 | 59.9 |
| 12 | 1,910 | 6.4 | 42.6 | 58.8 | 5.9 | 42.4 | 58.9 |
| 15 | 2,050 | 7.0 | 46.2 | 57.4 | 6.2 | 46.6 | 57.8 |
| 3 | 2,340 | ... | .... | .... | 6.1 | 41.9 | 56.9 |
| 9 | 3,030 | 7.1 | 44.4 | 54.8 | 6.3 | 44.1 | 54.8 |
| 6 | 3,360 | ... | .... | .... | 7.1 | 39.6 | 59.2 |
| 14 | 3,800 | 8.1 | 45.3 | 58.1 | 7.0 | 42.4 | 58.1 |
| 1 | 4,150 | 8.0 | 44.0 | 59.0 | ... | .... | .... |

that the water content of the bones decreases and that the percentage of ash remains practically constant from the beginning to the end of

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the fetal period. Since it is difficult to obtain a uniform ash composition, it is questionable whether any slight changes in the ash content should be emphasized.

Table 2 presents the data obtained from the chemical analyses of the long bones of twenty-one fetuses. The values for calcium, sodium

TABLE 2.—*Chemical Composition of Fetal Bone* *

| Fetus, No. | Weight, Gm. | Bone | Calcium | Phosphorus | Magnesium | Sodium | Chlorine | Potassium | Sulfur |
|---|---|---|---|---|---|---|---|---|---|
| 20 | 197 | Femur and tibia | 571.2 | 345.6 | 21.5 | 48.6 | .... | ... | ... |
| 11 | 650 | Femur | 514.3 | 315.8 | 16.7 | 27.4 | 11.3 | ... | ... |
| | | Tibia | 539.1 | 319.8 | 16.7 | 28.5 | .... | ... | ... |
| | | Humerus | 521.3 | 318.5 | 17.6 | 27.2 | .... | ... | ... |
| 16 | 660 | Femur | 602.0 | 354.4 | 19.9 | 26.7 | 8.6 | ... | ... |
| | | Tibia | 598.9 | 357.6 | 18.9 | 28.0 | .... | ... | ... |
| | | Humerus | 598.3 | 351.0 | 19.8 | 28.4 | .... | ... | ... |
| 7 | 680 | Femur | 587.9 | 366.1 | 17.3 | 39.3 | 10.5 | ... | ... |
| | | Tibia | 587.1 | 359.2 | 19.5 | 35.7 | .... | ... | ... |
| | | Humerus | 573.6 | 360.4 | 19.0 | 36.3 | .... | ... | ... |
| 13 | 760 | Femur | 571.6 | 350.2 | 19.6 | 25.4 | 8.3 | ... | ... |
| | | Tibia | 574.3 | 344.6 | 18.1 | 27.6 | 9.0 | ... | ... |
| 19 | 786 | Femur and tibia | 627.6 | 360.0 | 17.6 | 29.9 | .... | ... | ... |
| 18 | 800 | Femur | 557.0 | 332.2 | 19.6 | 27.6 | 9.9 | ... | ... |
| | | Tibia | 559.7 | 335.6 | 20.4 | 28.8 | 9.6 | ... | ... |
| 4 | 810 | Femur | 487.7 | 299.7 | 16.9 | 28.6 | .... | ... | ... |
| | | Tibia | 471.7 | 286.4 | 17.0 | 27.5 | 5.8 | ... | ... |
| 10 | 920 | Femur | 523.7 | 311.3 | 17.9 | 22.1 | 7.6 | ... | ... |
| | | Tibia | 510.4 | 306.8 | 16.1 | 22.3 | 8.5 | ... | ... |
| 8 | 1,230 | Femur | 525.0 | 330.4 | 17.4 | 26.1 | 8.5 | ... | ... |
| | | Tibia | 567.0 | 339.3 | 18.8 | 27.6 | .... | ... | ... |
| | | Humerus | 526.3 | 325.4 | 17.2 | 24.8 | 7.7 | ... | ... |
| 5 | 1,300 | Femur | 543.6 | 319.0 | 14.4 | 30.9 | 9.2 | 6.6 | ... |
| | | Tibia | 533.0 | 325.4 | 14.6 | 30.9 | 8.8 | 7.1 | ... |
| 21 | 1,310 | Femur | 586.3 | 346.4 | 16.3 | 25.3 | 6.9 | ... | ... |
| | | Tibia | 560.3 | 344.6 | 17.4 | 25.9 | 6.6 | ... | ... |
| 22 | 1,680 | Femur | 582.3 | 352.1 | 17.7 | 26.1 | 7.2 | ... | ... |
| | | Tibia | 597.0 | 348.3 | 18.2 | 26.5 | 7.9 | ... | ... |
| 12 | 1,910 | Femur | 581.0 | 337.4 | 17.3 | 26.4 | 7.2 | ... | ... |
| | | Tibia | 567.7 | 339.1 | 18.3 | 27.5 | 7.9 | ... | ... |
| 15 | 2,050 | Femur | 555.7 | 330.4 | 15.0 | 25.9 | 6.7 | ... | ... |
| | | Tibia | 562.3 | 330.4 | 16.4 | 26.5 | 7.8 | ... | ... |
| 3 | 2,340 | Tibia | 583.6 | 327.9 | 15.9 | 28.1 | 7.7 | 5.8 | ... |
| 9 | 3,030 | Femur | 535.7 | 319.0 | 15.3 | 26.2 | 7.1 | ... | ... |
| | | Tibia | 530.3 | 319.0 | 15.3 | 26.3 | 7.5 | ... | ... |
| 2 | 3,050 | Femur | 581.0 | 323.8 | 14.2 | 24.7 | 6.0 | 5.3 | ... |
| | | Tibia | 591.6 | 335.6 | 15.4 | 25.8 | 5.5 | 4.3 | 4.4 |
| 6 | 3,360 | Tibia | 566.3 | 346.4 | 16.4 | 25.5 | 6.2 | 5.3 | ... |
| 14 | 3,800 | Femur | 555.7 | 337.4 | 14.4 | 27.2 | 6.6 | ... | 6.3 |
| | | Tibia | 578.3 | 340.9 | 15.6 | 27.3 | 7.3 | ... | ... |
| 1 | 4,150 | Femur and tibia | 583.6 | 327.9 | 14.9 | 27.6 | 6.3 | ... | 5.4 |

* The values are given in millimols per hundred grams of dry substance.

and phosphorus remained constant, while the values for magnesium and chlorine decreased with growth.

Table 3 presents the physical constants and the chemical data on the epiphysial cartilage of seventeen fetuses. In cartilage, as in bone, there is a loss in the water content at birth with no apparent change in the percentage of ash. It is interesting that during the period of fetal

life, in which the water content of the body decreases 12 per cent, the water content of the bone and cartilage decreases about 3 per cent.

The minerals in cartilage differ considerably in content from those in bone. The data show that there is an excess of phosphorus over calcium. Undoubtedly a considerable percentage of this phosphorus is present in organic combination. A part of the organic phosphorus is contained in the lipid fraction of the cartilage. The total fat content

TABLE 3.—*Composition of the Epiphysial Cartilage of the Human Fetus* *

| Fetus, No. | Weight, Cm. | Water, Percentage | Ash, Percentage of Dry Weight | Calcium | Magnesium | Sodium | Potassium | Phosphorus | Chlorine | Sulfur |
|---|---|---|---|---|---|---|---|---|---|---|
| 11 | 650 | 85.5 | 11.5 | 9.4 | 5.4 | 111.4 | 38.6 | 13.3 | .... | .... |
| 16 | 660 | 86.5 | 11.4 | 10.5 | 5.1 | 102.6 | 44.4 | 17.0 | .... | .... |
| 13 | 760 | 85.3 | 11.6 | 11.0 | 4.6 | 109.4 | 38.2 | 15.5 | .... | .... |
| 18 | 800 | 86.7 | 12.1 | 8.7 | 4.5 | 124.5 | 37.5 | 13.3 | 38.8 | .... |
| 4 | 810 | 85.6 | 11.4 | 8.6 | 4.7 | 116.2 | 35.7 | 13.8 | .... | .... |
| 10 | 920 | 85.3 | 12.4 | 4.0 | 4.5 | 132.0 | 32.5 | 8.8 | .... | .... |
| 8 | 1,230 | 83.7 | 11.4 | 5.3 | 4.2 | 109.9 | 35.6 | 9.9 | 39.4 | .... |
| 5 | 1,300 | 84.7 | 9.9 | 5.6 | 4.1 | 88.2 | 41.6 | 11.7 | 27.9 | .... |
| 21 | 1,310 | 85.2 | 11.0 | 7.0 | 3.8 | 109.9 | 38.2 | 11.9 | 33.3 | .... |
| 22 | 1,680 | 85.6 | 11.9 | 7.6 | 3.7 | 132.9 | 28.6 | 14.8 | 30.1 | .... |
| 12 | 1,910 | 85.5 | 12.3 | 8.9 | 4.0 | 136.4 | 29.5 | 10.5 | 22.0 | .... |
| 15 | 2,050 | 84.3 | 11.0 | 9.9 | 3.7 | 113.0 | 35.0 | 7.7 | 20.4 | 52.5 |
| 3 | 2,340 | 83.6 | 10.2 | 6.1 | 3.7 | 104.9 | 30.4 | 8.1 | 26.2 | 45.3 |
| 9 | 3,030 | 83.9 | 11.2 | 10.8 | 3.5 | 108.0 | 27.9 | 9.6 | 38.1 | .... |
| 6 | 3,360 | 82.1 | 9.2 | 7.6 | 3.6 | 82.0 | 34.8 | 8.7 | 17.5 | 49.1 |
| 14 | 3,800 | 82.7 | 10.5 | 7.0 | 4.0 | 102.7 | 35.7 | 7.6 | 22.3 | 49.3 |
| 1 | 4,150 | 82.5 | 10.8 | 6.2 | 3.0 | 123.0 | 22.0 | 8.5 | 46.5 | .... |

* The values are given in millimols per hundred grams of dry substance.

TABLE 4.—*Composition of the Bone, the Cartilage and the Entire Body of the Infant at Birth* *

| | Sodium | Potassium | Chlorine | Calcium | Magnesium | Phosphorus | Nitrogen | Sulfur |
|---|---|---|---|---|---|---|---|---|
| Bone..... | 27.2 | 5.9 | 7.8 | 541.8 | 17.4 | 336.4 | 365.0 | 5.4 |
| Epiphysial cartilage. | 103.9 | 30.1 | 31.1 | 7.9 | 3.5 | 8.6 | 735.8 | 49.0 |
| Body at birth..... | 30.9 | 17.6 | 20.9 | 60.8 | 4.5 | 67.6 | 574.4 | 9.0 |

* The values are given in millimols per hundred grams of dry substance.

of bone averaged 4.6 per cent, with a lipid phosphorus content of less than 0.1 per cent of the total phosphorus. Similar analyses of cartilage gave from 9 to 12 per cent as the value for the total lipid content, with a lipid phosphorus content of 7 per cent of the total phosphorus.

In table 4 the average values for the concentrations of the minerals in the bone and the cartilage are compared with those for the whole body at birth. Marked differences are to be noted in the concentration of several minerals, particularly sodium and sulfur, in the cartilage.[2c]

SUMMARY

The femurs, the tibias and the epiphysial cartilage of twenty-one fetuses weighing from 197 to 4,150 Gm. were analyzed for the content of their mineral constituents.

Both bone and cartilage lose water during fetal life, and the magnesium and the chlorine content of bone show a significant decrease.

Comparative figures are given for the minerals found in the bone, the epiphysial cartilage and the entire body of the infant at birth.

Except for variations in the content of the minerals which are present in very small amounts, the proportion of the main inorganic elements in bone apparently changes but slightly in early life.

# RESPIRATORY METABOLISM IN INFANCY AND IN CHILDHOOD

## XX. THE NITROGEN METABOLISM IN PREMATURE INFANTS—COMPARATIVE STUDIES OF HUMAN MILK AND COW'S MILK

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In a previous study of the basal metabolism of premature infants [1] it was noted that when the infants were on a diet of human milk the nitrogen in the urine collected for short periods while the infants were in the respiratory chamber represented only 5 per cent of the total heat production.[2] When cow's milk was used, the urinary nitrogen increased to represent 17 per cent of the total calories.

These findings seemed to confirm the popular conception that the protein of human milk is better suited for retention by the growing human organism than the protein of cow's milk. This conclusion is, however, unwarranted, since the infants on the two types of diet received protein differing not only in quality but also in quantity.

Observations were therefore planned in which the retention of nitrogen by premature infants fed human milk and that by premature infants fed formulas of cow's milk of a similar caloric and protein content might be compared. The mixtures of cow's milk were modified by the addition of dextrimaltose, olive oil and water so that they approximated the human milk in protein, fat, carbohydrate and fluid content. In another series of observations the intake of protein in cow's milk was approximately doubled and quadrupled at the expense of the calories derived from fat. Such studies were desirable since there are in the

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From the New York Hospital and the Department of Pediatrics, Cornell University Medical College.

1. Gordon, H. H., and Levine, S. Z.: Respiratory Metabolism in Infancy and in Childhood: XVIII. The Respiratory Exchange in Premature Infants—Basal Metabolism, Am. J. Dis. Child. **52**:810 (Oct.) 1936.

2. $\frac{\text{urinary nitrogen (grams)} \times 26.51}{\text{total calories produced}} \times 100$. Lusk, G.: Science of Nutrition, ed. 3, Philadelphia, W. B. Saunders Company, 1923, p. 62.

literature, to our knowledge, no quantitative studies of the ability of premature infants to retain the nitrogen of cow's milk, the few available observations of the nitrogen balance having been made on infants receiving human milk.[3] Data were also collected on the absorption of nitrogen and of fat from the various preparations used.

## METHOD

Six healthy premature male infants (four white and two Negro) were studied. The clinical criteria of prematurity are given in table 1; the degree of prematurity as estimated from the expected date of birth varied from six to nine weeks and the weight at birth from 1,182 to 2,160 Gm. Urine and feces were collected separately in eighteen observations of from three to nine days, totaling ninety-one days, which with one exception (observation 3, table 2) followed foreperiods of constant diet of from three to seven days. Four infants (H. B., G. F., T. A. and W. S.) were studied in an air-conditioned nursery and two (G. and V. R.) in the metabolism pavilion of the children's clinic, where the temperature and the humidity fluctuated only slightly. The excretion of nitrogen through the skin was not measured, but since premature infants perspire little and since the temperature and the humidity of the environment were practically constant, such excretion was probably of little relative significance.

*Diets.*—All the formulas were prepared by the nurse in charge of the metabolism unit and were fed to the infants by her or by trained assistants. All the infants took their formulas well, with a minimum of regurgitation.

The mixtures of cow's milk consisted of varying amounts of powdered half skimmed milk, powdered whole milk, powdered whole lactic acid milk, evaporated milk or pasteurized whole milk, diluted with water and fortified with dextrimaltose, olive oil[4] or calcium paracaseinate. The ingredients were weighed accurately to within 0.1 Gm., and the mixture was divided equally into six or eight feedings.

The human milk in three observations (observations 2, 6 and 7, table 1) consisted of "canned" pooled mother's milk which had been preserved on ice after being heated to 100 C. for twenty minutes on each of three successive days. In observation 12, fresh pooled milk boiled twenty minutes was used, and in observation 13, pasteurized fresh pooled milk boiled five minutes. No raw human milk was used.

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3. (*a*) Langstein, L., and Niemann, A.: Ein Beitrag zur Kenntnis der Stoffwechselvorgänge in den ersten vierzehn Lebenstagen normaler und frühgeborener Säuglinge, Jahrb. f. Kinderh. **71**:604, 1910. (*b*) Schlossmann, A.: Ueber Menge, Art und Bedeutung des Phosphors in der Milch und über einige Schicksale desselben im Säuglingsorganismus, Arch. f. Kinderh. **40**:1, 1905. (*c*) Rubner, M., and Langstein, L.: Energie und Stoffwechsel zweier frühgeborener Säuglinge, Arch. f. Physiol. **39**:39, 1915. (*d*) Hamilton, B.: Calcium and Phosphorus Metabolism of Prematurely Born Infants, Acta pædiat. **2**:1, 1923. (*e*) Hamilton, B., and Moriarty, M.: The Composition of Growth in Infancy: I. A Premature Infant, Am. J. Dis. Child. **37**:1169 (June) 1929. (*f*) John, F.: Ueber den Eiweissansatz bei Frühgeburten, Ztschr. f. Kinderh. **51**:794, 1932. (*g*) Gulacsy, Z.: Nitrogen Metabolism of Premature Infants, Magyar orvosi arch. **33**:494, 1932.

4. (*a*) Holt, L. E., Jr.; Tidwell, H. C.; Kirk, C. M.; Cross, D. M., and Neale, S.: Studies in Fat Metabolism: I. Fat Absorption in Normal Infants, J. Pediat. **6**:427, 1935. (*b*) Tidwell, H. C.; Holt, L. E., Jr.; Farrow, H. L., and Neale, S.: II. Fat Absorption in Premature Infants and Twins, ibid. **6**:481, 1935.

TABLE 1.—*Clinical Criteria of Prematurity and Daily Diet of Infants*

| Subject | Weight at Birth, Gm.* | Estimated Degree of Prematurity, Weeks† | Observation | Age at Beginning of Observation, Days | Weight at Beginning of Observation, Gm. | Average Daily Gain in Weight, Gm. | Type of Milk in Diet | Total Fluid, Cc. | Protein,‡ Gm. | Fat, Gm. | Carbohydrate,§ Gm. | Calories,‖ Total | Percentage of Calories Derived from: Protein | Fat | Carbohydrate | Formula |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| G. | 2,160 | 6 | 1 | 21 | 2,720 | 44 | Cow's | 420 | 14.63 | 5.79 | 53.0 | 331 | 18 | 16 | 66 | Powdered half skimmed milk 50 Gm., dextrimaltose 30 Gm., $H_2O$ ad 420 cc. |
| V. R. | 1,754 | 9 | 2 | 21 | 1,960 | 23 | Human | 360 | 5.35 | 6.87 | 27.0 | 197 | 11 | 32 | 57 | "Canned" pooled human milk 360 cc. |
| | | | 3 | 26 | 2,050 | 40 | Cow's | 360 | 5.27 | 11.08 | 27.0 | 235 | 9 | 44 | 47 | Powdered half skimmed milk 18 Gm., dextrimaltose 19 Gm., olive oil 9 Gm., $H_2O$ ad 360 cc. |
| | | | 4 | 34 | 2,380 | 33 | Cow's | 400 | 11.70 | 9.63 | 30.4 | 262 | 18 | 34 | 48 | Powdered half skimmed milk 40 Gm., dextrimaltose 12 Gm., olive oil 5 Gm., $H_2O$ ad 400 cc. |
| | | | 5 | 40 | 2,600 | 20 | Cow's | 440 | 23.91 | 5.26 | 31.8 | 277 | 35 | 18 | 47 | Powdered half skimmed milk 43 Gm., dextrimaltose 12 Gm., calcium paracaseinate 14 Gm., $H_2O$ ad 440 cc. |
| | | | 6 | 48 | 2,800 | 35 | Human | 670¶ | 7.67 | 14.79 | 36.0 | 317 | 10 | 43 | 47 | "Canned" pooled human milk 480 cc., $H_2O$ 190 cc. |
| H. B. | 1,368 | 10 | 7 | 16 | 1,454 | 19 | Human | 320 | 4.99 | 9.38 | 24.0 | 206 | 10 | 42 | 48 | "Canned" pooled human milk 320 cc. |
| | | | 8 | 39 | 2,076 | 18 | Cow's | 360 | 6.14 | 11.43 | 29.7 | 253 | 10 | 42 | 48 | Powdered half skimmed milk 21 Gm., dextrimaltose 20 Gm., olive oil 9 Gm., $H_2O$ ad 360 cc. |
| | | | 9 | 53 | 2,588 | 17 | Cow's | 440 | 15.21 | 11.02 | 35.9 | 312 | 20 | 33 | 47 | Powdered half skimmed milk 52 Gm., dextrimaltose 12 Gm., olive oil 5 Gm., $H_2O$ ad 440 cc. |
| G. F.# | 1,182 | 7 | 10 | 34 | 1,506 | 30 | Cow's | 320 | 4.23 | 9.79 | 26.4 | 219 | 8 | 42 | 49 | Powdered whole lactic acid milk 18 Gm., dextrimaltose 20 Gm., olive oil 5 Gm., $H_2O$ ad 320 cc. |
| | | | 11 | 47 | 1,966 | 25 | Cow's | 360 | 5.85 | 10.96 | 34.2 | 266 | 9 | 38 | 53 | Powdered whole milk 23 Gm., dextrimaltose 26 Gm., olive oil 5 Gm., $H_2O$ ad 360 cc. |
| | | | 12 | 60 | 2,338 | 24 | Human | 480 | 7.31 | 14.13 | 36.0 | 309 | 10 | 43 | 48 | Fresh pooled human milk boiled 20 minutes 480 cc. |
| T. A. | 1,490 | 7 | 13 | 19 | 1,874 | 38 | Human | 360 | 4.44 | 12.37 | 28.4 | 250 | 7 | 46 | 47 | Pasteurized fresh human milk boiled 5 minutes 360 cc. |
| | | | 14** | 28 | 2,240 | 4 | Cow's | 400 | 7.21 | 12.65 | 34.9 | 290 | 10 | 41 | 49 | Pasteurized cow's milk boiled 5 minutes 210 cc., dextrimaltose 25 Gm., olive oil 5 Gm., $H_2O$ ad 400 cc. |
| | | | 15 | 34 | 2,258 | 29 | Cow's | 400 | 7.21 | 12.65 | 34.9 | 290 | 10 | 41 | 49 | Same as preceding formula |
| | | | 16 | 40 | 2,640 | 39 | Cow's | 455 | 11.99 | 14.55 | 36.5 | 334 | 15 | 41 | 45 | Evaporated milk 180 cc., dextrimaltose 18 Gm., $H_2O$ ad 455 cc. |
| | | | 17 | 50 | 2,922 | 17 | Cow's | 525 | 13.69 | 14.30 | 40.5 | 355 | 16 | 37 | 47 | Pasteurized cow's milk boiled 5 minutes 420 cc., dextrimaltose 21 Gm., $H_2O$ ad 525 cc. |
| W. J. | 1,700 | 9 | 18 | 19 | 1,884 | 20 | Cow's | 320 | 7.36 | 7.88 | 31.7 | 233 | 13 | 31 | 56 | Pasteurized cow's milk boiled 5 minutes 240 cc., dextrimaltose 20 Gm., $H_2O$ ad 320 cc. |

* All infants were less than 45 cm. long at birth.
† Prematurity was estimated from the record of the mother.
‡ Protein in Gm. = nitrogen in Gm. × 6.25.
§ Lactose was assumed to be 7.5 per cent of milk in observations 2, 6 and 7; the percentage of lactose was determined in all other instances.
‖ The number of calories was calculated by multiplying the number of grams of protein, of fat and of carbohydrate by the constants 4.1, 9.3 and 4.1, respectively.
# Twin.
¶ Each day 190 cc. of water was added because of watery stools.
** Diarrhea occurred during this observation. The feces were well formed in the next observation, in which the infant was on the same diet.

Thoroughly mixed samples of the powdered milk and pooled daily aliquot samples of the liquid cow's milk and human milk were analyzed for nitrogen, fat and lactose.[5] The calcium paracaseinate was analyzed for nitrogen.

The intake of protein, in grams, was determined by multiplying the dietary nitrogen by 6.25. The daily caloric intake was determined by multiplying the grams of protein, fat and carbohydrate by the respective constants 4.1, 9.3 and 4.1. The intake of fluid varied from 160 to 220 cc. (except in two observations, 1 and 6 in table 3); the dietary calories, from 100 to 132, and the ingested protein, from 2.25 to 9.06 Gm. per kilogram per twenty-four hours (table 3). The infants gained from 17 to 34 Gm. daily in all except one observation (observation 14, table 1), in which diarrhea occurred. Each infant received 20 drops of viosterol daily.

*Urine.*—The specimens of urine were collected for periods of approximately twenty-four hours with the aid of a metabolism mattress [6] modified to fit the regular bassinet for premature infants. Its surface measured 25 by 13 inches (63 by 13 cm.), and it had a cut-out 3 inches (7 cm.) in diameter for the stool container and an aperture below that for the glass connecting tube which ran from the small size specimen tube to a large flask containing toluene. The urine was analyzed for nitrogen, and the results were corrected for twenty-four hour periods.

*Feces.*—The stools were collected in individual containers and combined for periods of from three to five days. The pooled specimens were dried on a steam bath and analyzed for nitrogen and fat.

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5. The same methods were used for analyzing milk, urine and feces: the macro-Kjeldahl method in triplicate for nitrogen, the Roese-Gottlieb method (Association of Official Agricultural Chemists: Official and Tentative Methods of Analysis Compiled by the Committee on Editing Methods of Analysis, Washington, D. C., Association of Official Agricultural Chemists, 1930, p. 217) in duplicate for fat and the gravimetric method of the Association of Official Agricultural Chemists in triplicate for lactose (ibid., p. 216). Six analyses for nitrogen, six for fat and two for lactose were made on human milk; four determinations of nitrogen, four of fat and four of lactose were made on liquid cow's milk. The results, as well as the chemical analyses of the proprietary preparations, are presented in the following tabulation. The latter corresponded closely with the analyses submitted by the manufacturers.

| | Protein (Nitrogen × 6.25), Percentage | Fat, Percentage | Lactose, Percentage |
|---|---|---|---|
| Human milk | 1.44 (1.2-1.6) | 2.93 (1.9-3.4) | 7.63 (7.4-7.9) |
| Cow's milk | | | |
| I. Pasteurized | 3.19 (3.0-3.4) | 3.40 (3.2-3.6) | 4.76 (4.7-5.0) |
| II. Evaporated | 6.66 | 8.08 | 10.26 |
| III. Powdered | | | |
| Half skimmed milk (Dryco) | 29.25 | 11.57 | 45.95 |
| Whole milk (Klim) | 25.44 | 25.93 | 35.86 |
| Whole lactic acid milk (Mead Johnson & Co.) | 23.52 | 26.61 | 35.50 |
| Calcium paracaseinate (Casec) | 80.92 | | |

6. Hoag, L. A.: Apparatus for the Quantitative Collection of Urine and Stools in Male Infants, Am. J. Dis. Child. **44**:770 (Oct.) 1932.

† Prematurity was estimated from the record of the mother.
†† Protein in Gm. = nitrogen in Gm. × 6.25.
* Lactose was assumed to be 7.5 per cent of milk in observations 2, 6 and 7; the percentage of lactose was determined in all other instances.
** The number of calories was calculated by multiplying the number of grams of protein, of fat and of carbohydrate by the constants 4.1, 9.3 and 4.1, respectively.
*** Twin.
**** Each day one cc. of water was added because of watery stools. Formed in the last observation, in which the infant was on the same diet.

RESULTS

In table 2 the detailed results are presented in terms of twenty-four hours. The data are summarized in table 3. The nitrogen retained represents the nitrogen of the intake minus the fecal and the urinary nitrogen. For comparative purposes, it was calculated in terms of body weight and in relation to the nitrogen apparently absorbed from the gastro-intestinal tract.[7]

*Retention and Percentage of Utilization of the Nitrogen of Human Milk and of Cow's Milk.*—The retention of nitrogen in five observations on four premature infants fed human milk which contained an average of 119 calories and 2.77 Gm. of protein per kilogram per twenty-four hours averaged 0.246 Gm. per kilogram per twenty-four hours, with a percentage of utilization of 70.9 (table 4 and chart 1, column 1). With a diet of cow's milk of similar caloric and protein content, the retention of nitrogen and the percentage of utilization of four infants of comparable ages and weights were practically the same: 0.272 Gm. and 70.4 per cent. The ranges were likewise comparable: from 0.21 to 0.31 Gm. and from 64 to 80 per cent for human milk and from 0.23 to 0.29 Gm. and from 65 to 80 per cent for cow's milk. At this level of intake, generally regarded as well above the minimum, no differences in the retention of nitrogen were found in these short periods of study. This range compares favorably with the range of from 64 to 80 per cent calculated by us from the data of Langstein and Niemann,[3a] Schlossmann,[3b] Rubner and Langstein,[3c] Hamilton [3d] and John [3f] in ten observations on premature infants fed human milk. It is notably higher than

7. The shortness of the periods of observation made calculations of the retention in terms of gain in body weight [3e] of little significance. The ratio of nitrogen retained to nitrogen apparently absorbed, i. e., $\frac{\text{dietary nitrogen} - (\text{fecal} + \text{urinary nitrogen})}{\text{dietary nitrogen} - \text{fecal nitrogen}}$, is called the percentage of utilization. It seems a more valid measure of the ability of the tissues to retain nitrogen than does the customary ratio of nitrogen retained to nitrogen ingested. It was not deemed justifiable to subject premature infants to a nitrogen-free diet to determine the "endogenous" fecal and urinary nitrogen, the value for which was necessary for calculation of the biologic values, and the coefficients of true digestibility, for the protein of human and of cow's milk. H. H. Mitchell and T. S. Hamilton (The Biochemistry of the Amino Acids, American Chemical Society Monograph Series, New York, Chemical Catalog Company, Inc., 1929) stated that one can estimate the total physiologic effect of dietary protein by relating the amount of nitrogen apparently retained in the body for both growth and maintenance to the amount of dietary nitrogen apparently absorbed from the gastro-intestinal tract. Similarly, one can validly compare the cofficients of apparent digestibility obtained for these dietary substances, since the most important factors affecting the amount of "metabolic" nitrogen excreted in the feces are the amounts of dry food consumed and the concentration of indigestible carbohydrate (Mitchell and Hamilton).

TABLE 2.—*Detailed Results in Grams per Twenty-Four Hours*

| Subject | Observation | Date | Average Weight, Gm. | Fore-period, Days | Period of Study, Days | Type of Milk in Diet | Nitrogen | | | | | | | Fat | | | Dry Weight of Feces, Gm. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Intake (1), Gm. | Feces (2), Gm. | Urine (3) Average, Gm. | Urine (3) Range, Gm. | Absorbed (1 — 2), Gm. | Total Excreted (2 + 3), Gm. | Total Retained 1 — (2 + 3), Gm. | Intake (4), Gm. | Feces (5), Gm. | Absorbed (4 — 5), Gm. | |
| | | 1935 | | | | | | | | | | | | | | | |
| G. | 1 | 11/29-12/4 | 2,800 | 6 | 5 | Cow's | 2.3401 | 0.2393 | 1.0923 | (1.091-1.140) | 2.1008 | 1.3316 | 1.0085 | 5.785 | 1.801 | 3.984 | 5.962 |
| | | 1936 | | | | | | | | | | | | | | | |
| V. R. | 2 | 1/24- 1/27 | 1,967 | 3 | 3 | Human | 0.8554 | 0.1666 | 0.1978 | (0.195-0.201) | 0.6888 | 0.3644 | 0.4910 | 6.865 | 3.253 | 3.612 | 5.544 |
| | 3 | 1/29- 2/ 2 | 2,133 | 2 | 4 | Cow's | 0.8424 | 0.0936 | 0.2654 | (0.261-0.269) | 0.7488 | 0.3590 | 0.4834 | 11.083 | 3.762 | 7.321 | 4.548 |
| | 4 | 2/ 6- 2/ 9 | 2,407 | 4 | 3 | Cow's | 1.8720 | 0.1593 | 0.9133 | (0.891-0.932) | 1.7127 | 1.0726 | 0.7904 | 9.628 | 2.515 | 7.113 | 4.582 |
| | 5 | 2/12- 2/16 | 2,638 | 3 | 4 | Cow's | 3.8249 | 0.2512 | 2.3826 | (2.322-2.476) | 3.5737 | 2.6338 | 1.1911 | 5.255 | 1.299 | 3.956 | 4.318 |
| | 6 | 2/20- 2/24 | 2,818 | 4 | 4 | Human | 1.2269 | 0.2995 | 0.3335 | (0.324-0.348) | 0.9274 | 0.6330 | 0.5939 | 14.788 | 1.496 | 13.292 | 8.865 |
| H. B. | 7 | 3/31- 4/ 3 | 1,461 | 5 | 3 | Human | 0.7990 | 0.1808 | 0.1066 | (0,095-0.125) | 0.6182 | 0.2874 | 0.5116 | 9.378 | 4.966 | 4.412 | 7.647 |
| | | 4/ 7- 4/10 | 1,632 | 8 | 3 | Human | 0.7990 | 0.1981 | 0.1493 | (0.142-0.157) | 0.6009 | 0.3474 | 0.4516 | 9.378 | 4.958 | 4.420 | 8 373 |
| | | 4/13- 4/16 | 1,776 | 14 | 3 | Human | 0.7990 | 0.1362 | 0.1292 | (0.112-0.144) | 0.6628 | 0.2654 | 0.5336 | 9.378 | 4.733 | 4.645 | 5.712 |
| | 8 | 4/23- 4/27 | 2,121 | 7 | 4 | Cow's | 0.9828 | 0.0744 | 0.2430 | (0.236-0.263) | 0.9084 | 0.3174 | 0.6654 | 11.430 | 3.867 | 7.567 | 4.675 |
| | | 4/27- 4/30 | 2,186 | 11 | 3 | Cow's | 0.9828 | 0.0754 | 0.3188 | (0.292-0.357) | 0.9074 | 0.3942 | 0.5886 | 11.430 | 2.836 | 8.594 | 3.460 |
| | 9 | 5/ 7- 5/10 | 2,608 | 7 | 3 | Cow's | 2.4337 | 0.1446 | 1.1751 | (1.095-1.241) | 2.2891 | 1.3197 | 1.1140 | 11.021 | 2.800 | 8.221 | 4.128 |
| G. F. | 10 | 6/ 4- 6/ 6 | 1,550 | 6 | 2 | Cow's | 0.6773 | 0.0721 | 0.1236 | (0.121-0.126) | 0.6052 | 0.1957 | 0.4816 | 9.790 | 2.494 | 7.296 | 3.170 |
| | | 6/ 9- 6/12 | 1,781 | 11 | 3 | Cow's | 0.6773 | 0.0579 | 0.1244 | (0.121-0.127) | 0.6194 | 0.1823 | 0.4950 | 9.790 | 1.289 | 8.501 | 1.959 |
| | 11 | 6/17- 6/20 | 1,987 | 5 | 3 | Cow's | 0.9362 | 0.1182 | 0.2071 | (0.203-0.205) | 0.8180 | 0.3253 | 0.6109 | 10.964 | 4.814 | 6.150 | 5.891 |
| | | 6/20- 6/23 | 2,087 | 8 | 3 | Cow's | 0.9362 | 0.1613 | 0.2225 | (0.211-0.232) | 0.7749 | 0.3838 | 0.5524 | 10.964 | 7.774 | 3.190 | 9.374 |
| | 12 | 6/30- 7/ 3 | 2,361 | 5 | 3 | Human | 1.1688 | 0.2902 | 0.3202 | (0.294-0.354) | 0.8786 | 0.6104 | 0.5584 | 14.126 | 2.505 | 11.621 | 6.994 |
| T. A. | 13 | 9/ 8- 9/11 | 1,922 | 4 | 3 | Human | 0.7106 | 0.0856 | 0.1331 | (0.129-0.139) | 0.6250 | 0.2187 | 0.4919 | 12.368 | 2.189 | 10.179 | 3.430 |
| | | 9/11- 9/14 | 2,021 | 7 | 3 | Human | 0.7106 | 0.1681 | 0.1452 | (0.133-0.155) | 0.5425 | 0.3133 | 0.3973 | 12.368 | 3.801 | 8.567 | 5.507 |
| | 14 | 9/17- 9/19 | 2,225 | 3 | 2 | Cow's | 1.1540 | 0.3657 | 0.2182 | (0.217-0.219) | 0.7883 | 0.5839 | 0.5701 | 12.645 | 7.976 | 4.669 | 15.970 |
| | | 9/19- 9/23 | 2,192 | 5 | 4 | Cow's | 1.1540 | 0.3001 | 0.3058 | (0.259-0.345) | 0.8539 | 0.6059 | 0.5481 | 12.645 | 8.095 | 4.550 | 12.398 |
| | 15 | 9/23- 9/26 | 2,287 | 9 | 3 | Cow's | 1.1540 | 0.1837 | 0.3353 | (0.331-0.340) | 0.9703 | 0.5190 | 0.6350 | 12.645 | 6.869 | 5.776 | 8.806 |
| | 16 | 10/ 1-10/ 6 | 2,712 | 5 | 5 | Cow's | 1.9190 | 0.2592 | 0.8163 | (0.726-0.937) | 1.6598 | 1.0755 | 0.8435 | 14.546 | 2.929 | 11.617 | 6.234 |
| | 17 | 10/ 9-10/12 | 2,947 | 3 | 3 | Cow's | 2.1907 | 0.1292 | 1.3382 | (1.277-1.455) | 2.0615 | 1.4674 | 0.7233 | 14.299 | 4.020 | 10.279 | 5.592 |
| | | 10/12-10/15 | 3,025 | 6 | 3 | Cow's | 2.1907 | 0.1655 | 1.3382 | (1.329-1.357) | 2.0252 | 1.5047 | 0.6860 | 14.299 | 9.216 | 5.083 | 11.912 |
| W. J. | 18 | 12/21-12/24 | 1,913 | 6 | 3 | Cow's | 1.1441 | 0.0736 | 0.3626 | (0.308-0.426) | 1.0705 | 0.4362 | 0.7079 | 7.777 | 4.826 | 2.951 | 5.543 |
| | | 12/28-12/30 | 2,011 | 13 | 2 | Cow's | 1.1928 | 0.0824 | 0.4155 | (0.390-0.441) | 1.1104 | 0.4979 | 0.6949 | 7.933 | 5.424 | 2.509 | 6.877 |
| | | 12/30- 1/ 3 | 2,075 | 15 | 4 | Cow's | 1.1928 | 0.0037 | 0.5035 | (0.480-0.537) | 1.0991 | 0.5972 | 0.5906 | 7.933 | 5.235 | 2.698 | 6 430 |

TABLE 3.—*Summary of Results: Averages per Twenty-Four Hours*

| Subject | Observation | Average Weight, Gm. | Fore-period, Days | Period of Study, Days | Number of Periods | Diet: Type of Milk | Diet: Per Kg. per 24 Hours: Total, Cc. | Nitrogen, Gm. | Protein, Gm.* | Calories | N Retained / Body Weight: Gm. per Kg. per 24 Hr. | N Retained / N Intake: Percentage | N Retained / N Absorbed: Percentage† | N Absorbed / N Intake: Percentage‡ | Fat Absorbed / Fat Intake: Percentage‡ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| G. | 1 | 2,800 | 6 | 5 | 1 | Cow's | 150 | 0.836 | 5.22 | 118 | 0.360 | 43.1 | 48.0 | 89.8 | 68.9 |
| V. R. | 2 | 1,967 | 3 | 3 | 1 | Human | 183 | 0.435 | 2.72 | 100 | 0.250 | 57.4 | 71.3 | 80.5 | 52.6 |
| | 6 | 2,818 | 4 | 4 | 1 | Human | 238 | 0.435 | 2.72 | 112 | 0.211 | 48.4 | 64.0 | 75.6 | 89.9 |
| | 3 | 2,133 | 2 | 4 | 1 | Cow's | 169 | 0.395 | 2.47 | 110 | 0.227 | 57.4 | 64.6 | 88.9 | 66.1 |
| | 4 | 2,407 | 4 | 3 | 1 | Cow's | 166 | 0.778 | 4.86 | 109 | 0.332 | 42.7 | 46.7 | 91.5 | 73.9 |
| | 5 | 2,638 | 3 | 4 | 1 | Cow's | 167 | 1.450 | 9.06 | 105 | 0.452 | 31.1 | 33.3 | 93.4 | 75.3 |
| H. B. | 7 | 1,623 | 5 | 9 | 3 | Human | 197 | 0.492 | 3.08 | 127 | 0.307 | 62.4 | 79.5 | 78.5 | 47.9 |
| | 8 | 2,155 | 7 | 7 | 2 | Cow's | 167 | 0.456 | 2.85 | 117 | 0.291 | 63.8 | 69.1 | 92.4 | 70.9 |
| | 9 | 2,608 | 7 | 3 | 1 | Cow's | 169 | 0.933 | 5.83 | 120 | 0.427 | 45.6 | 48.7 | 94.1 | 74.6 |
| G. F. | 12 | 2,361 | 5 | 3 | 1 | Human | 203 | 0.495 | 3.09 | 131 | 0.237 | 47.8 | 63.6 | 75.2 | 82.3 |
| | 11 | 2,037 | 5 | 6 | 2 | Cow's | 177 | 0.460 | 2.87 | 131 | 0.286 | 62.2 | 73.0 | 85.1 | 42.6 |
| | 10 | 1,666 | 6 | 5 | 2 | Cow's | 191 | 0.407 | 2.55 | 131 | 0.293 | 72.1 | 79.7 | 90.4 | 80.7 |
| T. A. | 13 | 1,972 | 4 | 6 | 2 | Human | 183 | 0.360 | 2.25 | 127 | 0.225 | 62.6 | 76.2 | 82.1 | 75.8 |
| | 14§ | 2,203 | 3 | 6 | 2 | Cow's | 182 | 0.524 | 3.27 | 132 | 0.252 | 48.1 | 66.8 | 72.1 | 36.3 |
| | 15 | 2,287 | 9 | 3 | 1 | Cow's | 175 | 0.505 | 3.15 | 127 | 0.278 | 55.0 | 65.4 | 84.1 | 45.7 |
| | 16 | 2,712 | 5 | 5 | 1 | Cow's | 168 | 0.708 | 4.42 | 123 | 0.311 | 44.0 | 50.8 | 86.5 | 79.9 |
| | 17‖ | 2,986 | 3 | 6 | 2 | Cow's | 176 | 0.734 | 4.58 | 119 | 0.236 | 32.2 | 34.5 | 93.3 | 53.7 |
| W. J. | 18 | 2,007 | 6 | 9 | 3 | Cow's | 159 | 0.586 | 3.66 | 116 | 0.332 | 56.6 | 60.5 | 92.9 | 34.5 |

* Protein = nitrogen × 6.25.
† Percentage of utilization.
‡ Coefficient of apparent digestibility.
§ Omitted from averages in table 4 because of diarrhea.
‖ Omitted from averages in table 4 (compare footnote 9).

the average of 46 per cent (range, from 35 to 55 per cent) calculated from the data summarized by Czerny and Keller [8] for full term infants of comparable ages fed human milk.

TABLE 4.—*Average Retention of Nitrogen of Premature Infants Fed Human Milk and Cow's Milk*

| Type of Milk | Number of Observations | Average Duration of Fore-period, Days | Average Duration of Observation, Days | Average Weight, Gm. | Average Age at Beginning, Days | Intake of Nitrogen, Gm. per Kg. per 24 Hr. | Nitrogen Retained, Gm. per Kg. per 24 Hr. | Percentage of Utilization |
|---|---|---|---|---|---|---|---|---|
| Human..... | 5 | 4 | 5 | 2,148 | 33 | 0.443 | 0.246 | 70.9 |
| Cow's..... | 5 | 6 | 5 | 2,056 | 36 | 0.445 | 0.275 | 70.4 |
| Cow's..... | 5 | 6 | 5 | 2,507 | 33 | 0.773 | 0.352 | 50.9 |
| Cow's..... | 1 | 3 | 4 | 2,638 | 40 | 1.450 | 0.452 | 33.3 |

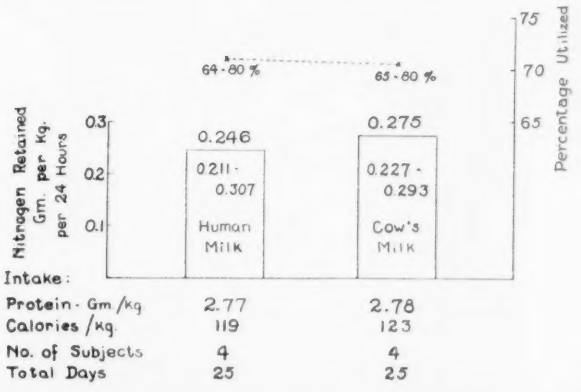


Chart 1.—Comparison of the retention and the percentage of utilization of nitrogen by premature infants of comparable average age and weight fed human milk and formulas of cow's milk of equivalent caloric and protein content. The vertical columns represent the retention of nitrogen in grams per kilogram per twenty-four hours. The broken line represents the percentage of utilization, i. e., the ratio of nitrogen retained to nitrogen absorbed.

Similar values for the retention of nitrogen for the various preparations of human milk and cow's milk were found, regardless of the antecedent processing. In no instance was raw milk fed, all products having been well heated during preparation.

*Effect of an Increase in the Intake of Protein (Cow's Milk) on the Retention of Nitrogen.*—An increase in the intake of protein without any increase in the dietary calories augmented the retention of nitrogen

8. Czerny, A., and Keller, A.: Des kindes Ernährung, Ernährungsstörungen und Ernährungstherapie, Vienna, Franz Deuticke, 1925, vol. 1, p. 691, table 249.

in six of seven observations[9] (table 4 and chart 2). Raising the average intake of protein from 2.8 to 4.8 Gm. per kilogram raised the amount of nitrogen retained from 0.275 to 0.352 Gm. per kilogram per twenty-four hours (chart 2, column 2). In a single observation, when the intake was 9.1 Gm. of protein per kilogram per twenty-four hours, the retention was 0.452 Gm. (chart 2, column 3).

The percentage of utilization fell from 70.5 to 50.9 and 33.3 at the higher levels of intake. This is in accord with the findings of Mitchell[10] and Forbes and his co-workers[11] for rats. The greater the excess of absorbed amino-acids over the requirements for growth and maintenance, the more the acids enter interchangeably with the fat and the carbohydrate into the energy exchange.[12]

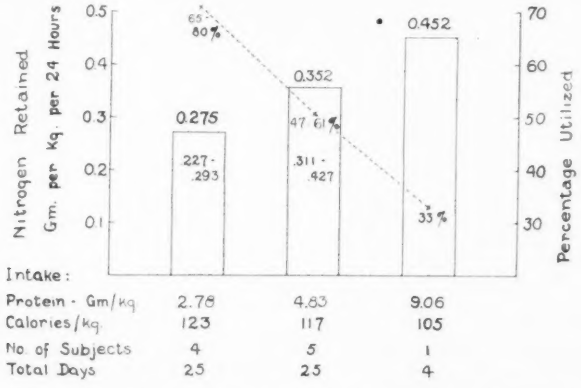


Chart 2.—The effect of increasing the protein ingested without increasing the dietary calories on the retention and the percentage of utilization of nitrogen by premature infants fed cow's milk. The vertical columns represent the retention of nitrogen in grams per kilogram per twenty-four hours. The broken line represents the percentage of utilization, i. e., the ratio of nitrogen retained to nitrogen absorbed.

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9. Observation 17 was omitted in computing the averages in table 4. In this observation, which was on the largest infant, who weighed 3,000 Gm. and was fed pasteurized cow's milk, the nitrogen retained was only 0.24 Gm. per kilogram per twenty-four hours and the percentage of utilization 35. Since no decrease in the retention of nitrogen from boiled pasteurized cow's milk was found in observations 15 and 18, the low retention in observation 17 may have been associated with the large size of the infant (table 7).

10. Mitchell, H. H.: The Biologic Value of Proteins at Different Levels of Intake, J. Biol. Chem. **58**:905, 1924.

11. Forbes, E. B.; Swift, R. W.; Black, A., and Kahlenberg, O. J.: The Utilization of Energy Producing Nutriment and Protein as Affected by Individual Nutrient Deficiencies, J. Nutrition **10**:461, 1935.

12. Mitchell, H. H., and Hamilton, T. S.: The Biochemistry of the Amino Acids, American Chemical Society Monograph Series, New York, Chemical Catalog Company, Inc., 1929.

*Absorption of Nitrogen from Human Milk and from Cow's Milk.*—The average percentage of dietary nitrogen apparently absorbed from the gastro-intestinal tract was 78.4 for human milk and 88.2 for mixtures of cow's milk with the same protein content (table 5). This difference of 10 per cent is not significant. Increasing the intake of protein to levels of 4.8 and 9.1 Gm. per kilogram resulted in similar high percentages of absorption (91.4 and 93.4).[13] Apparently no limit to the digestibility of the nitrogen of cow's milk was reached in short periods with the preparations used and within the specified range of intake of protein. These preparations included, as previously mentioned, pow-

TABLE 5.—*Absorption of Nitrogen from Human Milk and from Cow's Milk by Premature Infants*

| Type of Diet | Number of Observations | Average Age at Beginning, Days | Average Weight, Gm. | Intake of Protein, Gm. per Kg. per 24 Hr. | Coefficient of Apparent Digestibility* |
|---|---|---|---|---|---|
| Human milk | | | | | |
| "Canned" | 3 | 28 | 2,136 | 2.84 | 78.2 |
| Boiled 20 minutes | 1 | 60 | 2,361 | 3.09 | 75.2 |
| Pasteurized, boiled 5 minutes | 1 | 19 | 1,972 | 2.25 | 82.1 |
| Average | | 33 | 2,148 | 2.77 | 78.4 |
| Cow's milk | | | | | |
| Powdered half skimmed milk | 2 | 33 | 2,144 | 2.66 | 90.7 |
| Powdered whole milk | 1 | 47 | 2,037 | 2.87 | 85.1 |
| Powdered whole lactic acid milk | 1 | 34 | 1,666 | 2.55 | 90.4 |
| Pasteurized whole milk boiled 5 minutes | 1 | 28 | 2,203 | 3.27 | 72.1† |
| Pasteurized whole milk boiled 5 minutes | 1 | 34 | 2,287 | 3.15 | 84.1 |
| Average | | 36 | 2,056 | 2.78 | 88.2 |
| Powdered half skimmed milk | 3 | 36 | 2,605 | 5.30 | 91.8 |
| Evaporated milk | 1 | 40 | 2,712 | 4.42 | 86.5 |
| Pasteurized whole milk boiled 5 minutes | 2 | 35 | 2,497 | 4.12 | 93.1 |
| Average | | 36 | 2,587 | 4.76 | 91.4 |
| Powdered half skimmed milk plus calcium paracaseinate | 1 | 40 | 2,638 | 9.06 | 93.4 |

* $\frac{\text{Dietary nitrogen} - \text{fecal nitrogen}}{\text{Dietary nitrogen}}$

† Omitted from average because of diarrnea.

dered half skimmed milk, powdered whole milk, powdered whole lactic acid milk, boiled pasteurized cow's milk and evaporated milk (table 5). Similar findings for older full term infants were reported by Finkelstein and Jonas.[14]

*Absorption of Fat.*—In table 6 the infants are divided into three groups: (*a*) those receiving human milk, (*b*) those receiving cow's milk and (*c*) those receiving cow's milk plus olive oil. In each group the

13. The slightly higher results with the higher intakes may indicate that the fecal "endogenous" nitrogen (intestinal secretions plus bacteria) did not increase proportionally with the increase in the intake of nitrogen.

14. Finkelstein, H., and Jonas, W.: Zur Kenntnis des alimentären Fiebers: II. Der N-Stoffwechsel beim Eiweissenreicherungsfieber, Ztschr. f. Kinderh. **49**:55, 1930.

average intake of fat was approximately 5 Gm. per kilogram per twenty-four hours,[15] the average age at the beginning of the observations was approximately 35 days and the average weight varied from 2,150 to 2,570 Gm.

The average percentage of fat absorbed from human milk in five observations was 70 (range, 48 to 90). This figure is considerably below the average of 90 per cent quoted by Holt and his co-workers [4a]

TABLE 6.—*Absorption of Fat from Human Milk and from Cow's Milk by Premature Infants*

| Type of Diet | Observation | Age at Beginning, Days | Average Weight, Gm. | Intake of Fat, Gm. per Kg. per 24 Hr. | Coefficient of Apparent Digestibility,* Percentage | Dry Weight of Feces, Gm. per Kg. per 24 Hr. | Fecal Fat, Percentage of Dry Weight of Feces |
|---|---|---|---|---|---|---|---|
| **Human milk** | | | | | | | |
| "Canned" | 7 | 16 | 1,623 | 5.78 | 47.9 | 4.46 | 68 |
| Pasteurized, boiled 5 minutes | 13 | 19 | 1,972 | 6.27 | 75.8 | 2.27 | 67 |
| "Canned" | 2 | 21 | 1,967 | 3.49 | 52.6 | 2.82 | 59 |
| "Canned" | 6 | 48 | 2,818 | 5.25 | 89.9 | 3.14 | 17 |
| Boiled 20 minutes | 12 | 60 | 2,361 | 5.98 | 82.3 | 2.96 | 36 |
| Average | | 33 | 2,150 | 5.35 | 69.7 | | |
| **Cow's milk** | | | | | | | |
| Pasteurized, boiled 5 minutes | 18 | 16 | 2,006 | 3.93 | 34.5 | 3.13 | 82 |
| Evaporated | 16 | 40 | 2,712 | 5.37 | 79.9 | 2.30 | 47 |
| Pasteurized, boiled 5 minutes | 17 | 50 | 2,986 | 4.79 | 53.7 | 2.93 | 76 |
| Average | | 35 | 2,568 | 4.70 | 56.0 | | |
| **Cow's milk plus olive oil†** | | | | | | | |
| Powdered half skimmed milk | 3 | 26 | 2,133 | 5.19 | 66.1 | 2.13 | 83 |
| Powdered half skimmed milk | 4 | 34 | 2,407 | 4.00 | 73.9 | 1.90 | 55 |
| Powdered whole lactic acid milk | 10 | 34 | 1,666 | 5.88 | 80.7 | 1.54 | 74 |
| Pasteurized whole milk | 15 | 34 | 2,287 | 5.53 | 45.7 | 3.85 | 78 |
| Powdered half skimmed milk | 8 | 39 | 2,155 | 5.30 | 70.9 | 1.89 | 82 |
| Powdered whole milk | 11 | 47 | 2,037 | 5.38 | 42.6 | 3.86 | 80 |
| Powdered half skimmed milk | 9 | 53 | 2,608 | 4.23 | 74.6 | 1.58 | 68 |
| Average | | 38 | 2,185 | 5.07 | 64.9 | | |

* $\frac{\text{Dietary fat} - \text{fecal fat}}{\text{Dietary fat}}$

† From 40 to 50 per cent of the fat in the intake was in the form of olive oil except in observations 3 and 8, in which olive oil constituted 80 per cent of the fat of the intake.

for full term infants and confirms the findings of Rubner and Langstein [3c] and Hamilton [3d] that premature infants do not absorb fat from human milk as well as full term infants. Two of the three youngest

15. The similarity in intake permitted comparative use of the ratio of fat apparently absorbed to fat ingested, i. e., $\frac{\text{dietary minus fecal fat}}{\text{dietary fat}}$, although the "endogenous" excretion of fat was not determined. In general, under these conditions of fixed intake, the dry weight of the stools varied directly with the percentage of dietary fat excreted but the percentage of the dried stool represented by fat varied from 17 to 68 per cent for human milk and from 47 to 83 per cent for the formulas of cow's milk (table 6).

infants (observations 2 and 7) absorbed 48 and 53 per cent of the dietary fat, as compared with 82 and 90 per cent for the two oldest infants (observations 6 and 12).

The average figure obtained for the three observations on cow's milk was 56 per cent (range, from 35 to 80 per cent). This average is practically the same as that obtained by Holt and his co-workers [4b] in their larger series of observations on premature infants of comparable ages and weights who were fed butter fat. In the observations on cow's milk plus olive oil, we obtained an average of 65 per cent, which is intermediate between the figures of 58 and 72 per cent obtained by those investigators for butter fat and olive oil, respectively.

In the observations on pasteurized cow's milk boiled five minutes the average percentage of dietary fat absorbed was only 45 (range, from 35 to 54; observations 15, 17 and 18, table 6), as compared with 80 and 81 in single observations on evaporated milk and powdered whole lactic acid milk (observations 16 and 10) and 71 (range, from 66 to 75) on powdered half skimmed milk plus olive oil (observations 3, 4, 8 and 9, table 6). In only one of six observations on powdered milk (observation 11, table 6) was a low percentage, 43, obtained. This is in accord with the opinion of Brennemann [16] on the benefits of prolonged heating on the formation of curd. Though few in number, these observations suggest that the fat of evaporated or powdered cow's milk is better absorbed by premature infants than the fat of ordinary pasteurized cow's milk boiled five minutes.

The number of observations is too few and the range of results too wide for one to attach significance to the average difference of 14 per cent between the absorption of fat from human milk and that from cow's milk. The results, however, confirm the finding that premature infants do not absorb fat from either human milk or cow's milk as well as full term infants.[17]

## COMMENT

The finding that when human milk and mixtures of cow's milk were fed to premature infants in amounts which gave equivalent, adequate calories and protein the same amounts of nitrogen were retained led to a closer examination of the claim that the protein of human milk is superior for retention by the growing human organism. Human milk has relatively more lactalbumin than cow's milk, and it has been shown that lactalbumin promotes growth in rats more effectively than casein.[18]

16. Brennemann, J.: The Curd and the Buffer in Infant Feeding, J. A. M. A. **92**:364 (Feb. 2) 1929.

17. Holt and others.[4] Rubner and Langstein.[3c] Hamilton.[3d]

18. Osborne, T. B., and Mendel, L. F.: A Quantitative Comparison of Casein, Lactalbumin and Edestin for Growth or Maintenance, J. Biol. Chem. **26**:1, 1916.

Furthermore, Edelstein and Langstein [19] found that the substitution of lactalbumin for casein in the diets of full term infants led to higher percentages of retention of nitrogen. In experiments in which human milk and cow's milk are compared, however, one feeds in each instance neither lactalbumin nor casein alone but mixtures of the two. In the observations here reported, in which the level of feeding was well above that generally regarded as a minimum, the essential amino-acids may have adequately supplemented each other to permit similar amounts of nitrogen to be retained.

If the minimal amount of protein is ingested or if the periods are longer, the proportion of the various amino-acids in human milk may render it more suitable for the storage of nitrogen by the growing human organism, but at a customary level of feeding for premature infants no differences were found between the retention of nitrogen by infants receiving human milk and that of infants receiving cow's milk for periods lasting as long as two weeks.

This finding is in accord with the opinion of Orgler [20] expressed in 1908 for full term infants and seems the only fair conclusion that one may draw from the later observations of Edelstein and Langstein.[19]

These observations are not to be construed as a disagreement with the clinical impression that human milk is better suited for the feeding of premature infants than cow's milk.[21] In longer periods of observation, differences in the retention of nitrogen or significant differences in health due to varied biologic properties might be demonstrated. Differences in the mineral content of the two types of milk, previously suggested as a cause for gastro-intestinal disorders in full term infants,[22] may be of greater significance in the case of premature infants.[23]

In table 7 the percentages for the utilization of nitrogen by individual infants are arranged according to the weight of the infants at the time of observation. In each instance the percentage of utilization is higher the smaller the infant at the time of observation. An augmented impulse toward growth inherent in the smaller infants may explain the fact that the percentage of utilization was higher for the premature than for the

19. Edelstein, F., and Langstein, L.: Das Eiweissproblem im Säuglingsalter, Ztschr. f. Kinderh. **20**:112, 1919.

20. Orgler, A.: Der Eiweiss-stoffwechsel des Säuglings, Ergebn. d. inn. Med. u. Kinderh. **2**:464, 1908.

21. Report of the Committee on Growth and Development: III. Nutrition, White House Conference on Child Health and Protection, New York, D. Appleton-Century Company, Inc., 1932.

22. (*a*) Finkelstein, H.: Lehrbuch der Säuglingskrankheiten, ed. 3, Berlin, Julius Springer, 1924, p. 209. (*b*) Meyer, L. F.: Die Bedeutung der Mineralsalze bei den Ernährungsstörungen des Säuglings, Jahrb. f. Kinderh. **71**:1, 1910.

23. Observations testing this hypothesis are being made.

full term infants. It may also account for the ability of young premature infants on equicaloric diets of higher protein content to retain increasing amounts of nitrogen, a result which Harrison [24] did not observe in older full term babies.

In contrast with the unimpaired ability of the premature infants to absorb the nitrogen of human milk and that of cow's milk, as compared with the ability of full term infants, a defect was observed in their absorption of fat. In some instances the fecal fat represented over 50 per cent of the dietary fat. With formulas of a composition analogous to that of human milk, in which approximately 40 per cent of the calories are derived from fat, 20 per cent of the total caloric intake might be lost as fat in the feces. This defective absorption of fat may explain

TABLE 7.—*Effect of Weight and Age on Percentage of Utilization of Nitrogen by Individual Infants*

| Subject | Observation | Diet | | | Age at Beginning, Days | Weight, Gm. | Percentage of Utilization |
|---|---|---|---|---|---|---|---|
| | | Type of Milk | Calories per Kg. per 24 Hr. | Protein, Gm. per Kg. per 24 Hr. | | | |
| V. R. | 2 | Human | 100 | 2.72 | 21 | 1,967 | 71.3 |
| | 3 | Cow's | 110 | 2.47 | 26 | 2,133 | 64.6 |
| | 6 | Human | 112 | 2.72 | 48 | 2,818 | 64.0 |
| H. B. | 7 | Human | 127 | 3.08 | 16 | 1,623 | 79.5 |
| | 8 | Cow's | 117 | 2.85 | 39 | 2,155 | 69.1 |
| G. F. | 10 | Cow's | 131 | 2.55 | 34 | 1,666 | 79.7 |
| | 11 | Cow's | 131 | 2.87 | 47 | 2,037 | 73.0 |
| | 12 | Human | 131 | 3.09 | 60 | 2,361 | 63.6 |
| T. A. | 13 | Human | 127 | 2.25 | 19 | 1,972 | 76.2 |
| | 15 | Cow's | 127 | 3.15 | 34 | 2,287 | 65.4 |
| T. A. | 16 | Cow's | 123 | 4.42 | 40 | 2,712 | 50.8 |
| | 17 | Cow's | 119 | 4.58 | 50 | 2,986 | 34.5 |

the failure of some premature infants to thrive on a caloric intake such as is usually deemed adequate.

## SUMMARY AND CONCLUSIONS

Balance studies of nitrogen and fat were made on six healthy premature boys ranging in age from 16 to 34 days and in weight from 1,454 to 2,720 Gm. at the beginning of the observations. The urine and the feces were collected separately in eighteen observations of from three to nine days (totaling ninety-one days) following foreperiods of constant diet of from three to seven days.

Four infants were fed equicaloric diets of human milk and mixtures of cow's milk which gave about 120 calories and 2.75 Gm. of protein per kilogram per twenty-four hours. The average amount of nitrogen

24. Harrison, H. E.: The Retentions of Nitrogen, Calcium and Phosphorus of Infants Fed Sweetened Condensed Milk, J. Pediat. **8**:415, 1936.

retained in these short periods was 0.25 Gm. per kilogram per twenty-four hours for the infants receiving human milk and 0.27 Gm. for the infants receiving cow's milk, and the percentages of utilization were 70.9 and 70.5, respectively. These percentages are considerably higher than those reported for full term infants under comparable conditions.

Increasing the intake of protein in mixtures of cow's milk to an average of 4.8 Gm. per kilogram per twenty-four hours for five infants and to 9.1 Gm. for one infant without increasing the caloric content of the diet augmented the nitrogen retained to 0.36 and 0.45 Gm. per kilogram per twenty-four hours. The percentages of utilization dropped to 51 and 33, respectively.

No defect in the absorption of nitrogen from human milk or from cow's milk was found, the coefficients of apparent digestibility ranging from approximately 80 to 90 per cent. The absorption of fat from both human milk and cow's milk was found to be less than that reported for full term infants.

DISCUSSION

DR. A. ASHLEY WEECH, New York: Although it is not possible to measure the metabolic nitrogen in the feces of the very young infant, I should like to point out that inability to include an allowance for this factor in the calculation of absorbed nitrogen means that the actual retentions must have been even higher than those recorded. This statement is not a criticism, since the comparisons were made on comparable data; it is mentioned only because one should not underestimate the completeness of digestion of milk protein in the infant.

DR. S. Z. LEVINE, New York: It is obvious that in order to determine the metabolic nitrogen one would have to put these infants on a nitrogen-free diet, and obviously this would be rather hazardous.

# Case Reports

## SICKLE CELL ANEMIA

### CHANGES IN THE VESSELS AND IN THE BONES

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MAPLEWOOD, N. J.

The purpose of this report is to record in the literature by means of visual impressions two further diagnostic features in the syndrome of sickle cell anemia, which were brought out in two cases that I have observed. These are, first, the so-called hair on end appearance in roentgenograms taken of the skulls of patients with long-standing involvement and, secondly, widespread vascular changes.

Roentgenograms showing similar changes have been published in roentgenologic journals (Rose,[1] Grinnan,[2] Vogt and Diamond,[3] Le Wald [4]), but so far only verbal descriptions have been given in clinical journals, except by Moore.[5] The vascular changes have not previously been described, as far as I have been able to discover.

The roentgenograms of the skulls of my patients showed an increase in the thickness of the calvarium in all areas. There was a loss of continuity of the outer table of the skull. The marrow cavity had been replaced by radially placed bone formations simulating many individual hair shafts standing erect (fig. 3). On gross examination the condition of the skull was classified as tower skull (Le Wald [4]), with its increase in height and corresponding decrease in lateral diameter. There was also flattening of the frontal bones. Postmortem examinations made

1. Rose, C. B.: Some Unusual X-Ray Findings in Skulls, Radiology **13**: 508, 1929.

2. Grinnan, A. C.: Roentgenologic Bone Changes in Sickle Cell and Erythroblastic Anemia: Report of Nine Cases, Am. J. Roentgenol. **34**:297, 1935.

3. Vogt, E. C., and Diamond, L. K.: Congenital Anemias, Roentgenologically Considered, Am. J. Roentgenol. **23**:625, 1930.

4. Le Wald, L. T.: Roentgen Evidence of Osseous Manifestations in Sickle Cell (Drepanocytic) Anemia and in Mediterranean (Erythroblastic) Anemia, Radiology **18**:792, 1932.

5. Moore, S.: Bone Changes in Sickle Cell Anemia with Note on Similar Changes Observed in Skulls of Ancient Mayan Indians, J. Missouri M. A. **26**: 561, 1929.

by Cooley [6] and Koch and Shapiro [7] in cases of erythroblastic anemia (in which roentgenograms of the skull were similar) showed also generalized thickening of the skull. The convex surface of the parietal bone showed a stippled or spongelike appearance due to the fact that the red marrow was seen through the very thin outer table, the erect hairlike

Fig. 1.—Photograph of patient C. M., showing the increase in the height of the skull and the resultant flattening of the frontal region and narrowing of the bitemporal distance. In the lateral view it can be seen more clearly that the height of the skull above the eyes and the ears is greatly increased.

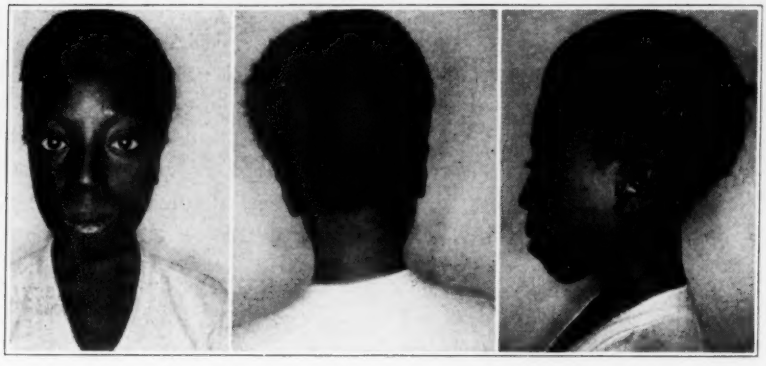

Fig. 2.—Photograph of C. M.'s brother, showing, particularly in the lateral view, much greater height above the ears and more marked flattening of the frontal region than in C. M.

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6. Cooley, T. B.; Witwer, E. R., and Lee, P.: Anemia in Children with Splenomegaly and Peculiar Changes in Bone, Am. J. Dis. Child. **34**:347 (Sept.) 1927.

7. Koch, L. P., and Shapiro, B.: Erythroblastic Anemia: Review of Cases Reported Showing Roentgenographic Changes in Bones and Five Additional Cases, Am. J. Dis. Child. **44**:318 (Aug.) 1932.

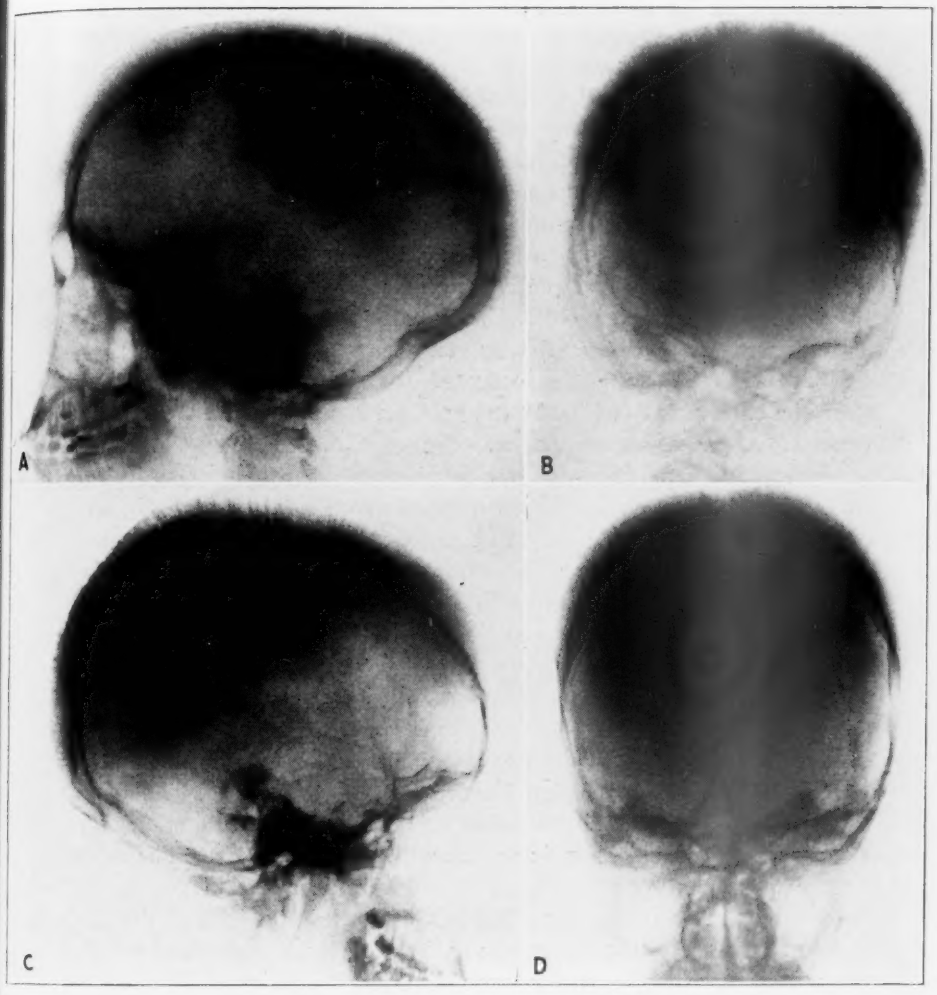


Fig. 3.—Roentgenograms of C. M.'s skull. *A*, the left lateral view, showing marked thickening, almost complete absence of the outer table, thinning of the inner table as the marrow cavity thickens and radially distributed bone columns separated by portions of the marrow cavity. *B*, the postero-anterior view, showing the extreme height of the radially placed bony trabeculae in the parietal regions. *C*, the right lateral view, showing almost total loss of the outer table except in the parietal region. The hair on end formation reaches the extreme thickness of 1½ inches (3.8 cm.). The bones at the base of the skull are decalcified and not hypertrophied in such a way as to close the foramina and cause the circulatory findings shown in figure 4. *D*, the anteroposterior view, showing that the thickness of the hair on end formation varies, being narrower on the sides and thicker on the top and stopping at the superior longitudinal suture, where the marrow cavity is absent.

formations appearing as bony points in this view. On section these areas of red marrow were seen to alternate with the radially placed bony trabeculae.

Graham [8] and Cooley [6] examined microscopically skulls affected by erythroblastic anemia. They noted between the two cortical areas an anastomosing network of broad bony trabeculae between which was cellular marrow. There was some replacement of the marrow by connective tissue, denoting beginning exhaustion. Later, vertical striation of the trabeculae appeared, as the marrow cavity became nearly exhausted by overstimulation and was replaced by bone (Whipple [9] and Karshner [10]). Whipple and Bradford [11] observed a patient with erythroblastic anemia and had serial roentgenograms of the skull made; they observed that these changes occurred two years and seven months after the child was born. The external periosteal layer of bone, while present under the microscope, was distinctly thinned by pressure due to tremendous hypertrophy of the bone marrow.

The long bones on roentgen examination showed moderate thinning of the cortex, with diffuse coarse irregular trabeculation of the medullary cavity, most marked near the ends of the bones. Pathologically, Graham [8] observed the same condition, and in addition the central third of the cortex was honeycombed with dense bony columns interspersed with dark red areas of marrow.

The eyegrounds in both the cases reported here had an abnormal vascular appearance (fig. 4). The veins were greatly dilated and at the same time tortuous. The arteries also were tortuous, but not to so great an extent. There was no sign of edema of the nerve head. There was crossing of the veins and arteries at an oblique angle, without the compression which would occur in vessels with thickened walls. The caliber of the vessels decreased evenly and not irregularly, as in vessels with diseased walls. Since no bony changes occurred in the base of the skull, the foramina were thought to be unaffected. It was therefore felt that the vessels were congenitally abnormal. The superficial temporal vessels were also extremely tortuous and thickened. Since these two groups of vessels were abnormal, could not the remaining vessels of the skull, including the diploic veins, also have been affected, thus causing the pathologic diploic development?

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8. Graham, G. S.: Sickle Cell Anemia with Necropsy, Arch. Int. Med. **34**: 778 (Dec.) 1924.

9. Whipple, A. O.; Reeves, R. J., and Cobb, C. C.: Atypical Haemolytic Anemia with Splenomegaly in Children, Ann. Surg. **88**:330, 1928.

10. Karshner, R. G.: Roentgen Studies of Bones in Certain Diseases in the Blood of Infants, Am. J. Roentgenol. **20**:433, 1928.

11. Whipple, G. H., and Bradford, W. L.: Racial or Family Anemia of Children Associated with Fundamental Disturbances of Bone and Pigment Metabolism (Cooley-Von Jaksch), Am. J. Dis. Child. **44**:336 (Aug.) 1932.

REPORT OF CASES

C. M., a 9 year old Negro boy, was admitted to the service of Dr. R. Hunter Scott, of Newark City Hospital. He was to have had an operation for hydrocele, but the routine preoperative urinalysis showed a 3 plus reaction for albumin (a result which never could be corroborated). In the physical examination it was noted that the scleras were icteric, the skull was abnormal in outline and the vessels of the eyegrounds, particularly the veins, were abnormally tortuous. The superficial temporal vessels were also abnormally thickened, tortuous and distended. The spleen was not palpable. The blood pressure was slightly elevated (120 systolic and 86 diastolic). The red blood cells showed 90 per cent sickling in fifteen minutes (fig. 5). There were marked anemia, a blood count showing 42 per cent hemoglobin, 2,100,000 red cells, 12,630 white cells, 45 per

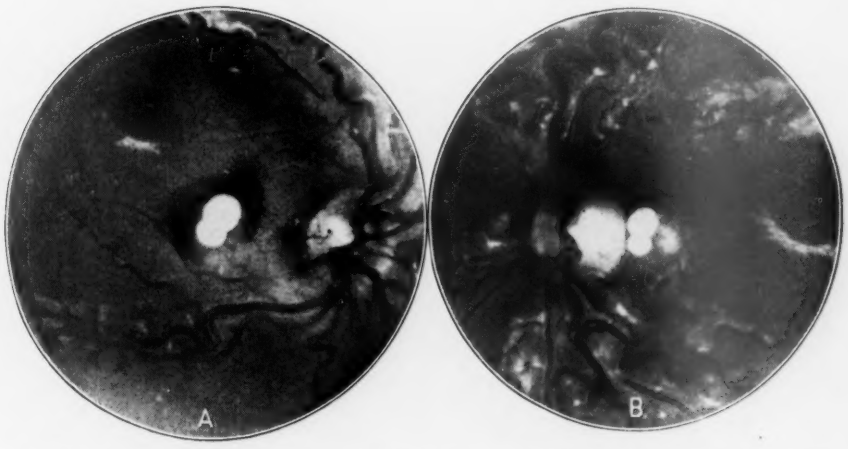


Fig. 4.—*A,* photograph of the right retina of C. M., showing tortuosity and dilatation of the vessels. The disk has a slight physiologic haziness of the nasal border. The nasal vessels pass obliquely and not at right angles, as thick-walled vessels would. The vessels decrease normally in caliber and not irregularly, in the manner of damaged vessels. *B,* photograph of the left retina of C. M., showing the increase in vascularity. The dilatation and tortuosity have affected all the vessels, the veins more than the arteries, even to the tiny vessels going to the macular region. The vessel walls are of normal thickness, the disk is normal and there is no exudate. The white areas are light reflexes. The two white dots in the center are the electrodes of the light used in obtaining the photograph.

cent polymorphonuclears, 27 per cent lymphocytes, 4 per cent endothelial leukocytes, 13 per cent eosinophils, 1 per cent basophils, 10 per cent juvenile myelocytes and 9.5 per cent reticulocytes. Additional specimens of urine always gave negative results except for a low fixed specific gravity, of 1.008 to 1.014. Chemical examination of the blood showed chlorides 0.528 per cent, sugar 0.095 per cent and urea nitrogen 11 mg. and cholesterol 310 mg. per hundred cubic centimeters. The icteric index was 15. The fragility test showed that hemolysis began with a 0.36 per cent solution of sodium chloride and was complete with a 0.14 per cent solution. The mean corpuscular volume was 76 cubic microns and the mean corpuscular hemoglobin 29 micromicrograms. The volume of packed red

Fig. 5.—Photomicrograph of a specimen of C. M.'s blood, which showed 90 per cent sickling in fifteen minutes. The narrowing and pointing of the ends of the cells are noteworthy. Examination of the blood showed hemoglobin 42 per cent, red cells 2,100,000, white cells 12,630, polymorphonuclears 45 per cent, lymphocytes 27 per cent, endothelial leukocytes 4 per cent, eosinophils 13 per cent, basophils 1 per cent, juvenile myelocytes 10 per cent and reticulocytes 9.5 per cent.

cells was 16 cc. per hundred cubic centimeters. The sedimentation rate corrected for anemia was 33 mm. in sixty minutes, the bleeding time was four minutes and the clot retraction time was fourteen hours.

On further inquiry into the patient's history it was brought out that he had had repeated attacks of pains in the joints, had always been thin and had grown tired and short of breath easily. He had a brother who, although younger, was suffering from the same complaints together with repeated attacks of abdominal pain. He showed the same changes in the vessels and skull, and his blood sickled in thirty minutes. These two children had the same father and mother. Other children, who had the same mother but a different father, did not show these changes. The mother said her family had always lived in Virginia. The patient's father said his family had always lived in North Carolina.

Roentgen changes similar to the ones described have been found in the skulls of ancient Mayan Indians (Vogt and Diamond,[3] Moore [5]) and in 2 or 3 per cent of the skulls of Peruvian mummies studied (Williams,[12] Feingold and Case [13]). They were also found in the skulls of certain tribes of Indians who lived in the region that is now the state of New York two hundred years ago. These skulls were principally children's skulls. The opinion has been ventured that this condition may have brought about the disappearance of the ancient Peruvian civilization.

## SUMMARY

Two cases of sickle cell anemia are reported with photographs and roentgenograms of the skull and retinal photographs.

Two new diagnostic features are added to the syndrome known as sickle cell anemia.

Dr. Harrison S. Martland made the reproductions of the roentgenograms and the photographs. Dr. William H. Hahn obtained the direct photographs of C. M.'s retinas.

536 Ridgewood Road.

12. Williams, H. U.: Human Paleopathology, with Some Original Observations on Symmetrical Osteoporosis of the Skull, Arch. Path. **7**:839 (May) 1929.

13. Feingold, B. F., and Case, J. T.: Roentgenologic Skull Changes in Anemias of Childhood: Report of a Case; a Few Notes on Similar Findings Among Skulls of Peruvian Indians, Am. J. Roentgenol. **29**:194, 1933.

# HEMORRHAGE IN A NEWLY BORN INFANT, CAUSING INTESTINAL AND BILIARY OBSTRUCTION

## REPORT OF A CASE WITH NECROPSY

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This report deals with the occurrence of fatal hemorrhage in a Negro boy who died at the age of 7 days. The hemorrhagic diathesis which he showed could not be definitely identified, since it did not conform to the criteria which are generally required in order that a diagnosis of hemorrhagic disease of the newly born, hemophilia, syphilis or sepsis be made.

A description of our case follows:

### REPORT OF CASE

*History.*—V. B., a Negro boy born March 10, 1934, was admitted to the Babies Hospital on March 11 and died on March 17. The chief complaint on admission was vomiting of blood. The patient was the eighth in his family. Four children were living and well. One child had died at 1 year of age of a "cold," another at 2 days of pneumonia and a third at 3 days of "infantile anemia of von Jaksch's disease," according to the report of the hospital where his death occurred.

The mother had had syphilis for an indefinite time. Her Wassermann reaction was strongly positive in January 1934. She had received two injections of neoarsphenamine in February 1934. The patient was a full term infant, born at home by spontaneous delivery. His condition was good until eighteen hours after birth when he began to vomit blood. This was described both as dark red and as resembling coffee-grounds. Vomiting continued up to the time of admission, and occurred every few minutes in small amounts. The infant appeared somewhat lethargic, but he nursed well. Petechiae were first noticed on his face shortly before he was brought to the hospital.

*Physical Examination* (on Admission, Thirty Hours After Birth).—The temperature was 99 F. The weight was 4,500 Gm. The patient was well developed and well nourished and appeared acutely ill. There were a large ecchymotic area, 2.5 by 2 cm., in the region of the left shoulder, a few smaller ecchymotic spots over the body, and numerous petechiae on the face. A small amount of clotted blood was present in the throat. The eyegrounds were normal. The heart and lungs showed nothing abnormal. The abdomen was slightly distended; neither the liver nor the spleen was felt. During the examination the infant vomited 30 cc. of dark brown material resembling coffee-grounds.

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From the Babies Hospital, New York.

Chemical analysis of the blood showed: bilirubin, 11.4 mg. per hundred cubic centimeters of serum, and fibrinogen, 0.83 per cent. The van den Bergh reaction was: direct 2 plus, indirect plus. The urine had a specific gravity of 1.032 and contained a heavy trace of albumin; there were from 1 to 6 red blood cells per high power field on two examinations. It gave a 4 plus reaction to the benzidine test on the day before the patient's death. The blood serum gave a negative reaction to the Kahn test. Culture of the blood on March 14 showed no growth. Stools gave a positive reaction for occult blood on two occasions. A test for bile pigment in the stool was negative. The vomitus gave a positive reaction for blood on two occasions. The hematologic findings are shown in the table.

The temperature reached 103 F. or more on the second, third and fourth days after admission, was subnormal on the fifth day, rose to 100.5 F. on the sixth day and reached normal on the day of death.

*Examinations of the Blood*

| Date, 1934 | Hemoglobin | Red Cells, per Cu.Mm. | Platelets, per Cu.Mm. | White Cells, per Cu.Mm. | Polymorphonuclears, Percentage | Lymphocytes, Percentage | Mononuclears, Percentage | Reticulocytes, Percentage of Red Cells | Bleeding Time, Minutes | Clotting Time, Minutes |
|---|---|---|---|---|---|---|---|---|---|---|
| 3/11 | | | | | | | | | 5 | 20+ |
| | 1. Transfusion 60 cc. | | | | | | | | | |
| | 2. Transfusion 60 cc. | | | | | | | | | |
| 3/12 | 11.0 Gm. (65% Sahli) | 2,720,000 | 712,000 | 15,400 | 75 | 24 | 1 | 9.6 | 3 | 10 |
| | 3. Transfusion 40 cc. | | | | | | | | | |
| 3/13 | 15.3 Gm. (90% Sahli) | 3,980,000 | 864,000 | 15,700 | 84 | 15 | 1 | 9.0 | .. | 6 |
| 3/14 | 17.9 Gm. (105% Sahli) | 4,760,000 | 888,000 | 14,000 | 87 | 13 | .. | 6.7 | .. | 5 |
| 3/16 | 16.5 Gm. (97% Sahli) | 4,000,000 | 928,000 | 12,950 | 67 | 32 | .. | 7.8 | .. | 20 |

*Roentgen Examination.*—In films the pulmonary fields appeared normal, though the cardiac shadow was slightly displaced to the left. On fluoroscopy the respiratory amplitude was small but approximately equal on the two sides. The pulmonary fields appeared clear. The cardiac shadow was of normal size but circular. There was no roentgenographic evidence of diaphragmatic paralysis.

*Course.*—On March 11 the child was given a transfusion of 60 cc. of whole blood from the father. He continued to vomit brownish fluid containing bright red blood on March 12, and he also had fresh clotted blood at the edges of his nostrils. He presented the picture of mild shock. Another transfusion of 60 cc. of whole blood from his father was given.

On March 13 the patient continued to bleed from his nose, stomach and intestines. A transfusion of 40 cc. of whole blood was given from another donor.

On March 14 the infant vomited a considerable quantity of dark brown fluid. The vomiting had become projectile. There was icterus of the scleras. The liver was palpated 4.5 cm. below the costal margin, and the spleen was easily felt. Dehydration was marked, and a clysis of 50 cc. of physiologic solution of sodium chloride was given. On March 15 bleeding from the stomach and intes-

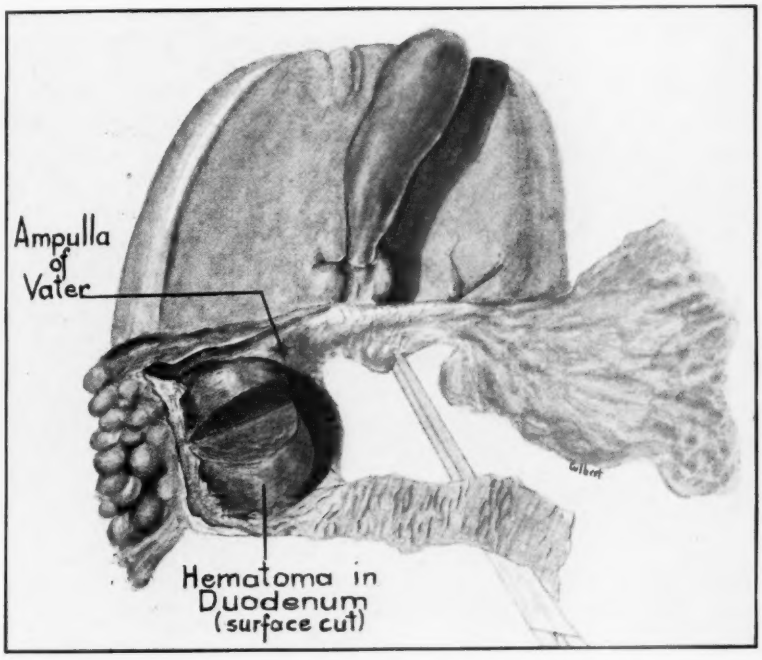
tines continued, but seemed less severe. The icterus increased in intensity. A clysis of 100 cc. of physiologic solution of sodium chloride was given. On March 16 the patient's condition was unchanged. A clysis of 80 cc. of physiologic solution of sodium chloride was given.

On March 17 the sites of the wounds made in transfusion bled profusely. An attempt to administer a fourth transfusion was unsuccessful, and the infant died soon afterward.

*Necropsy.*—Gross Examination: Autopsy was performed five and one-half hours after death. The anatomic diagnoses were hematoma of the duodenum, with obstruction of the intestines and of the common bile duct at the ampulla of Vater, jaundice, hemoperitoneum, subcutaneous, subpleural and pulmonary hemorrhages, accidental involution of the thymus, uric acid infarcts in the kidneys, patent foramen ovale and patent ductus arteriosus.

The body was normally developed, well nourished and icteric. There was a purpuric rash on the face and the trunk. Ecchymotic areas surrounded surgical incisions on the upper and lower extremities and wounds made by puncture on the back and the heels. At the junction of the stump of the umbilicus and the skin there was a small excoriation. The umbilical vein and the hypogastric arteries were free from exudate. The peritoneal cavity was filled with dark red fluid blood, which contained a few soft clots. The stomach and the duodenum were dilated, and in the latter, 3.5 cm. below the pyloric ring, a dark red ovoid mass, 3.5 by 2.5 by 2 cm., projected into the lumen, almost completely occluding it, as shown in the illustration. This mass was covered by intestinal mucosa without ulceration and on section proved to be composed of blood, lying mainly in the submucosa of the duodenum, though the outer margin of the hemorrhage was not sharply demarcated and in places the outer layers of the duodenal wall could not be identified. The hematoma compressed the ampulla of Vater, but the orifice of the common bile duct was patent. The common, hepatic and cystic ducts and the gallbladder were dilated, and the last was filled with dark green bile. The liver was of normal size and deeply stained with bile. Below the site of obstruction the small intestine was collapsed and free from blood. The colon was normal; it contained grayish or black fecal matter, but no fresh blood. The spleen weighed 6 Gm. and was normal on section. The lungs were anemic and icteric, with small pulmonary and subpleural hemorrhages, ranging from 0.5 to 2 cm. in diameter. The other viscera and the serous and mucous membranes were icteric; the foramen ovale and the ductus arteriosus were patent, and the thymus weighed 2 Gm.

Microscopic Examination: The hemorrhage in the duodenum was limited internally by intestinal mucosa. Externally, however, it was only in part surrounded by duodenal muscularis, which in some regions was infiltrated with polymorphonuclear leukocytes. In a widespread area blood had penetrated through the muscle layers into the adipose tissue of the neighboring mesentery and into the pancreas, where erythrocytes filled the interlobular septums. Into the periphery of the blood clot fibroblasts were penetrating from the surrounding structures. No lesions were demonstrable in the blood vessels. In the remainder of the duodenum small hemorrhages were scattered through the submucosa and the serosa. Many mononuclear cells, showing erythrophagocytosis, and small numbers of polymorphonuclear leukocytes had collected in the sinuses of the adjacent lymph nodes. There was no cholangeitis or cirrhosis in the liver, but the biliary canaliculi were distended by small bile plugs, and there was bile in some of the small bile ducts and Kupffer cells. Attached to the capsule of the spleen by a zone of proliferating fibroblasts was a blood clot. In the kidney a capsular space in one glomerulus




Hematoma in duodenum, resulting in duodenal and biliary obstruction.

was filled with erythrocytes, and the adjoining convoluted tubules were filled with blood. In addition to many erythrocytes in the pulmonary alveoli, there were scattered patches of lobular pneumonia.

## COMMENT

The time of onset and the sites of bleeding in this infant fit into the picture of hemorrhagic disease of the newly born, but the fact that bleeding continued after three transfusions from two different donors is much against this diagnosis. In forty-two cases of conditions diagnosed as hemorrhagic disease of the newly born at the Sloane Hospital for Women, New York, in only one were two transfusions necessary before the bleeding stopped. The fact that in the present case the coagulation time, which was twenty minutes on the second day of life and dropped to five minutes on the fourth, subsequently rose to twenty minutes on the sixth day suggests that the condition was some other disease. It has been stated [1] that hemophilia is rare in the early months of life. The only other case in our experience in which bleeding from hemophilia occurred early was that of a full term boy born in the Sloane Hospital for Women in February 1933. He was entirely normal until the eleventh day of life. After circumcision he bled profusely from the wound. His bleeding time was one minute, and two determinations of the coagulation time gave results of three and one-half and four and one-half minutes. After transfusion there was no further bleeding until the seventh postoperative day, when the circumcision wound bled a little. At that time the bleeding time was one and one-half minutes, and the clotting time was eight minutes. A Kahn test was negative. At 7 weeks of age the infant was brought to the clinic with a swollen right elbow. The roentgenogram showed a widened joint space and swelling of the soft tissue consistent with hemarthrosis. A diagnosis of hemophilia was made. The coagulation time was four and one-half minutes at that time. At 14 months of age the boy suffered a cut with a razor blade in his right shin, and he bled from this wound for three days. At about this time his coagulation time was fourteen minutes. When the boy was 15 months of age his gums were bruised, and they bled profusely. His only other admission to the outpatient department was at the age of 3½ years, when he attended the dermatologic clinic, where a diagnosis of infantile eczema was made. There were no complaints referable to hemophilia at that time.

In this case the possibility of a late manifestation of hemorrhagic disease and subsequent development of hemophilia have to be considered. Among the forty-two cases of hemorrhagic disease previously men-

1. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, ed. 10, revised by L. E. Holt Jr. and R. McIntosh, New York, D. Appleton-Century Company, 1933.

tioned there was one other in which the first manifestations of the disease appeared on the eleventh day of life, when the infant bled from a circumcision wound. His coagulation time was five and one-half minutes before transfusion and four minutes after transfusion. He could not be followed after the age of 1 month. The more cases of bleeding in the neonatal period or in the early months of life which one studies carefully, the more one feels that there are certain ones in which the condition does not correspond to any recognized clinical entity.

In the case which we are reporting, syphilis had to be carefully ruled out on account of the mother's positive Wassermann reaction. The infant's Kahn reaction was negative. It is possible that, if the child had lived longer, this reaction might have become positive. However, at autopsy no syphilitic lesions were found, so that it seems possible to exclude this diagnosis. Sepsis can be ruled out by the negative culture of the blood and by the observations at autopsy, since there was no pathologic evidence to support this diagnosis. From the clinical and hematologic findings, hemophilia seems the most probable diagnosis, but on account of the patient's age at death (7 days) this cannot be established with certainty.

SUMMARY

A case of fatal bleeding in a 7 day old Negro boy is reported. An unusual finding was the large hematoma in the duodenum, which resulted in intestinal obstruction; the extravasation was so located in relation to the ampulla of Vater that it also resulted in an obstruction to the common bile duct. This accounted for the marked icterus observed clinically.

In explanation of the underlying cause of hemorrhage, the suggested diagnosis of early hemophilia rests on the patient's failure to respond to transfusion, a phenomenon not observed in neonatal hemorrhagic disease. Serologic tests and observations at autopsy ruled out syphilis; sepsis was excluded by a negative culture of the blood and by the absence of infection pathologically.

Drs. Katharine Merritt and Rustin McIntosh assisted in the presentation of the foregoing case.

# MEDIASTINAL TERATOMA IN A CHILD SEVEN MONTHS OLD

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The discovery of dermoids in children is rare. This is particularly true of dermoid or teratoma of the mediastinum. There are nevertheless physical signs and certain chemical and roentgenologic procedures which materially aid in their recognition. The following case of mediastinal teratoma in a child 7 months old presented striking physical and roentgenologic findings which led to a conclusive preoperative diagnosis.

## REPORT OF A CASE

*History.*—A 7 month old white girl was referred to the department of pediatrics on Oct. 16, 1936, because of loss of weight, dyspnea and cough of three months' duration. There had been no vomiting and no record of fever in this period.

The patient was the youngest of four children living and well. There was no family history of tuberculosis or syphilis. The birth was normal, and the initial weight was 7 pounds (3,175 Gm.). She had been on a formula from birth. This was taken well, and she gained steadily up to the age of 4 months, when her best weight was 12 pounds and 5 ounces (5,594 Gm.). At that time, the symptoms developed for which she was referred to the hospital.

On the child's admission to the hospital her weight was 10 pounds and 15 ounces (4,951 Gm.), the temperature 102 F. and the respiratory rate 50. She appeared well developed but poorly nourished. She had a wide-eyed, anxious expression and was breathing with moderate difficulty. From time to time there was a harsh, nonproductive cough. The physical findings of importance were confined to the thorax and the head. The veins over these areas were prominent. The left side of the chest showed a distinct bulge, while over this area anteriorly and posteriorly the percussion note was flat. No pulsation was visible, and breath sounds were absent over the area of flatness. On the right side resonance was increased and the breath sounds were exaggerated. The heart sounds were normal, although the left border could not be distinguished from the flatness over the left side of the chest. The regional lymph nodes were not enlarged. The rest of the physical findings were negative.

*Laboratory Data.*—On October 17 examination of the blood showed hemoglobin 83 per cent (Sahli), red blood cells 4,220,000 and white blood cells 7,000, with polymorphonuclears 42 per cent, lymphocytes 56 per cent and mononuclears 2 per cent. A smear showed no organisms.

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The urine was normal. The Mantoux reaction to old tuberculin in dilutions of 1:1,000 and 1:100 was negative. The Wassermann and the Kahn reaction were negative.

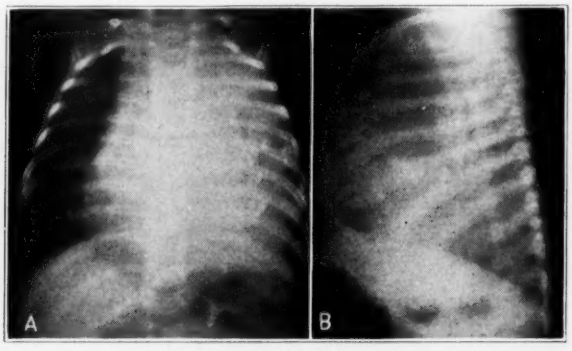


Fig. 1.—The anteroposterior view shows displacement of the trachea toward the right, narrowed interspaces on the left and calcareous deposits in the left side of the chest. The lateral view indicates the presence of the tumor in the anterior mediastinum. A mediastinal dermoid is usually found in this location.

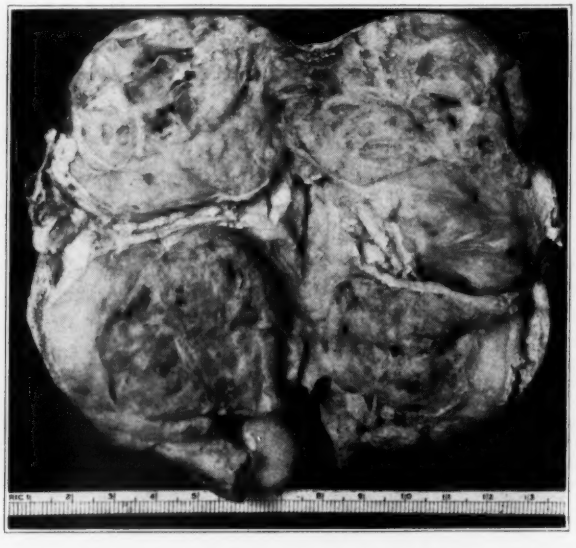

Fig. 2.—The appearance of the tumor after surgical removal. It weighed 225 Gm. and measured 12 by 8 by 3 cm.

*Preliminary Diagnosis.*—Although there was no history of preceding infection of the respiratory tract, owing to the temperature at the time of the child's admission and the flatness on physical examination, encapsulated empyema was considered first. Because the percussion note had a solid quality in spite of the

normal temperature after the first day in the hospital and because of roentgenologic evidence of multiple irregular calcareous deposits in the left side of the thorax, the presence of a dermoid was suspected (fig. 1).

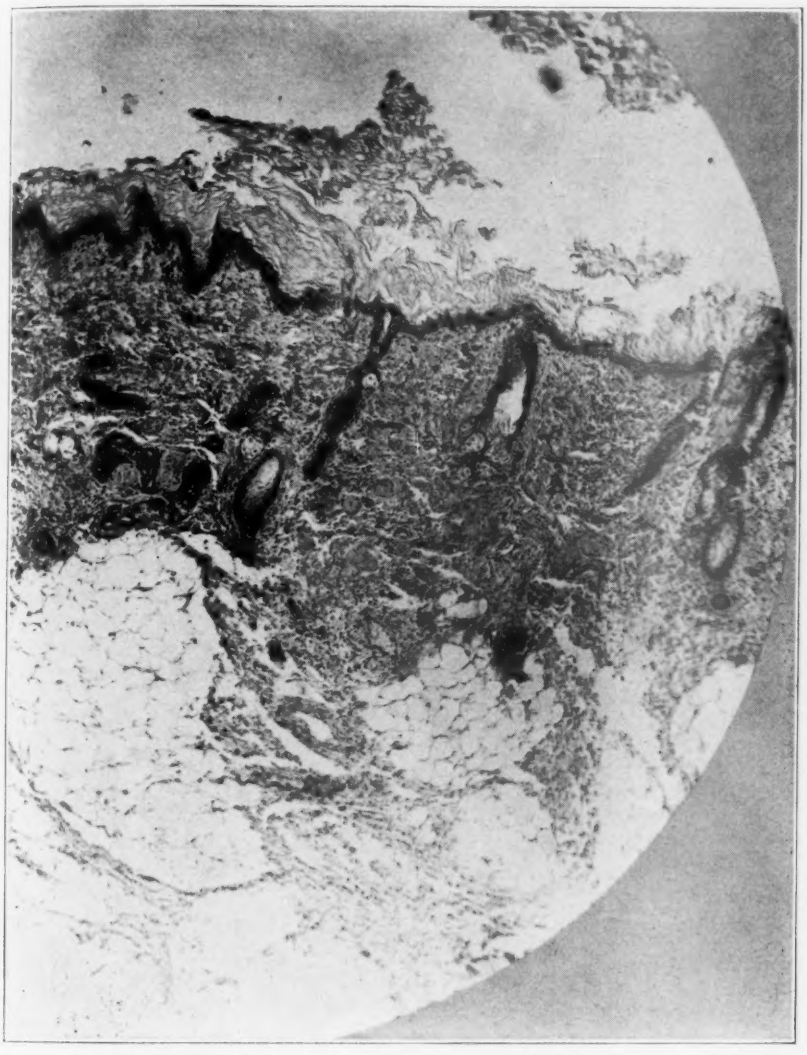

Fig. 3.—Photomicrograph showing the ectodermal elements of the tumor. Note the thin epidermis with hair follicles, sweat glands, sebaceous glands and smooth muscle elements beneath it.

*Course.*—A thoracentesis on October 21 returned 15 cc. of sterile thick grumous material, varying in color from brown to buff. The cholesterol content of this fluid was 320 mg. per hundred cubic centimeters. Minute fragments of columnar epithelium were found on microscopic examination. An Aschheim-Zondek test

gave negative results. After a transfusion of 80 cc. of whole blood and preliminary rib resection, the patient was operated on with intratracheal anesthesia on October 26. When the chest was opened, a large tumor, weighing 225 Gm.,

Fig. 4.—This shows the bone found in the tumor, with red blood cells and mature white blood cells in the marrow.

was found occupying the left side of the thorax. The tumor arose from the anterior mediastinum and had encroached on the left lung, so that it was com-

pletely collapsed. In spite of its large size, the tumor shelled out rather easily. In the course of the operation, which took about twenty minutes, the child went into shock. She improved temporarily after a blood transfusion, but after returning to the ward she sank rapidly and died three hours after operation.

Fig. 5.—This view shows columnar cells of the mucous type which suggest the respiratory tract. Glial tissue may be seen beneath the epithelium. There are some spicules of bone in the upper right corner.

*Pathologic Report.*—Macroscopic examination showed three specimens weighing together 225 Gm. The largest was egg shaped and measured 12 by 8 by 3

cm. (fig. 2). The irregularly lobulated surface was covered by a vascular, thin connective tissue capsule. Where the capsule was torn, a skinlike pink membrane covered the lobules. On section greenish yellow sebaceous material containing numerous fine hairs was found.

*Microscopic Examination* (figs. 3, 4 and 5).—Tissues were found which arose from all three embryonal layers.

1. The ectoderm was represented by several types of tissue. The skinlike membrane described grossly was made up of a thin epidermis and a thick keratin layer. All the layers of the normal squamous epithelium were found. In the cutis-like tissue beneath the epidermis were hair follicles and associated structures (sweat glands, sebaceous glands and elements of smooth muscle). In the connective tissue were ligamentous tissue and islands of bone. Nerve cells, glial tissue and salivary glands were identified among the other ectodermal derivatives.

2. The mesodermal elements were represented by smooth muscle and bone. In the marrow red blood cells and mature white blood cells were seen.

3. The entoderm was represented by tubules lined with columnar epithelium of the mucous type. The epithelium in some areas suggested that of the respiratory tract, being pseudostratified and lined with cilia.

No evidence of malignant degeneration was found in the tumor.

*Autopsy.*—Autopsy showed that the tumor had been completely removed but that a 50 Gm. blood clot was in the left pleural cavity. There was a tear in the superior mediastinum 3.5 by 1.5 cm., and the small blood vessels in this region were filled with clot, apparently the site of hemorrhage. The rest of the autopsy, both gross and microscopic, showed essentially normal organs.

## COMMENT

There is difference of opinion concerning the source of extragenital teratomas. Ewing [1] expressed the belief that a thoracic teratoma is produced by the growth of an aberrant sex cell or metastasis from a primary testicular tumor. It has been suggested that a dermoid may be due to the invagination of the ectoderm at the time of closure of the primitive wall of the thorax. This, however, will explain only derivatives of ectodermal tissue. Other theories, which suggest that a dermoid may originate from the thymus or the thyroid gland, branchial clefts or bronchi, may be criticized for the same reason; that is, they fail to account for a tumor that may contain three types of embryonal tissue. MacCallum [2] expressed the belief that one hypothesis will satisfactorily explain teratoma. He pointed out that a blastomere, which is the name given to a cell in the early stages of development after fertilization, may produce a teratoma of any degree of complexity. The complexity depends on the stage of segmentation at which the blastomere becomes separated from the main embryo.

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1. Ewing, James: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1922, p. 961.

2. MacCallum, W. G.: A Text-Book of Pathology, Philadelphia, W. B. Saunders Company, 1920, p. 1079.

These theories offer some explanation for the presence of teratoma, but they do not explain why this potpourri of tissue may lie dormant and insignificant in size for years before producing symptoms.

Hertzler,[3] who wrote one of the earliest reviews of the subject in 1916, likened the dermoid to the wen in the way it may suddenly increase in size. He suggested that degenerative changes occurring in the material of the cyst may irritate the sac, causing it to increase in size either through the production of more fluid or by cellular proliferation.

The number of reports in the literature of cases of mediastinal teratoma is increasing.[4] The reason for this would seem to be the aid given in diagnosis of thoracic tumor by roentgenograms [5] as well as the improvement in thoracic surgical technic.[6] In addition, more attention is paid to the identification of the various tissue elements which may compose a dermoid. Hertzler [3] was able to discover reports of 72 cases of dermoid cyst of the mediastinum in the literature in his time. Twenty-three years later, Hedblom [7] was able to add 113 to make a total of 185 cases. Recently Phemister [5] stated that there had been 208 cases up to July 1936. Of these, 48 were instances of teratoma. In Hertzler's series there were 4 dermoids of the mediastinum in patients under 10 years. Hedblom reported 22 cases of dermoid in the same region in children under 12 years. He did not state what percentage of the growths were teratomas, but since for all age groups it was 23 per cent, it seems reasonable that the number must be small. It remains a rather curious fact that a dermoid of the mediastinum or of any other enclosed cavity of the body is rarely recognized in childhood.

A dermoid generally makes its presence known only when it begins to increase in size. When it does, it is possible to recognize it in childhood. A 3 year old child, one of Hedblom's patients, was nearly asphyxiated by rapid growth of a tumor over a space of four months. Hedblom pointed out, however, that the onset of symptoms in three quarters of the 185 cases he reviewed was insidious. In 60 per cent

3. Hertzler, A. E.: Dermoids of the Mediastinum, Am. J. M. Sc. **152**:165 (Aug.) 1916.

4. (*a*) Wood, W. B.: Intrathoracic Cysts, Tubercle **17**:364, 1936. (*b*) Moir, P. J.: Dermoid Cysts of the Mediastinum, Brit. M. J. **1**:463, 1936. (*c*) Houghton, J. D.: Malignant Teratoma of Mediastinum, Am. J. Path. **12**: 349, 1936. (*d*) Teratoma, Anterior Mediastinum, Cabot Case 20411, New England J. Med. **211**:689 (Oct. 11) 1934.

5. Phemister, D. B.; Steen, W. B., and Volderauer, J. C.: Roentgenologic Criterion of Dermoid Cysts, Am. J. Roentgenol. **36**:14 (July) 1936.

6. Harrington, S. W.: Treatment in Eleven Cases of Mediastinal and Intrathoracic Teratomas, J. Thoracic Surg. **3**:50 (Oct.) 1933.

7. Hedblom, C. A.: Dermoid Cysts and Teratomata, J. Thoracic Surg. **3**: 22 (Oct.) 1933.

the duration of symptoms was under a year. In this case the symptoms were of three months' duration at the time of the infant's admission to the hospital. The first sign was failure to gain in weight associated with anorexia. This was followed by rapid respiration and the development of an occasional harsh, nonproductive cough. Cough and dyspnea are considered the commonest symptoms, occurring twice as often as any other complaint. Hedblom, in his excellent review, showed that there is nothing in the symptomatology which is of much help in recognizing a dermoid or a teratoma of the mediastinum. Should the patient cough up hair, which is sometimes done, of course, the diagnosis is facilitated.

### PHYSICAL SIGNS

It is common to note impaired resonance on physical examination of the chest.[8] It was a striking feature in this case. The percussion note was extremely flat, especially over the left anterior portion of the chest. It suggested the presence of the tumor, although before roentgen examination encapsulated empyema could not be excluded. The left side of the anterior wall of the chest bulged, and this has been noted in 33 per cent of the reported cases. Dilatation of the superficial veins of the thoracic wall suggested some mediastinal obstruction. However, it is not possible generally to diagnose such a tumor without the aid of roentgenograms, thoracentesis and sometimes pneumothorax.

The roentgenogram in this case (fig. 1) showed a dense shadow filling the left thoracic cavity, with some displacement of the heart to the right. Irregular flecks of calcium scattered through the anterior part of the left side of the chest and the fact that the tumor seemed to arise from the anterior mediastinum were evidence in favor of the diagnosis of dermoid cyst. A dermoid characteristically is located in the anterior mediastinum.[9] I was not able to demonstrate in the films the fluid level which Phemister [5] has recently described as present in some cases of dermoid of the chest. Thoracentesis practically clinched the diagnosis of a dermoid, because of the high cholesterol content of the aspirated fluid. An Aschheim-Zondek test was made on the baby's urine, because it has been found useful in the diagnosis of teratoma of the testicle, but the result was negative. This was perhaps due to the fact that the technic which Ferguson [10] has recommended was not employed.

It is not within the province of this paper to discuss in detail the surgical treatment of mediastinal dermoid. Harrington,[6] Hedblom [7] and

8. Harrington.[6] Hedblom.[7]

9. Churchill, E. D., in discussion on Teratoma, Anterior Mediastinum,[4d] p. 690.

10. Ferguson, R. S.: Quantitative Behavior of Prolan A in Teratoma Testis, Am. J. Cancer **18**:269 (June) 1933.

Eloesser [11] described various methods for reaching such a growth. All authorities agree that complete removal of the tumor is desirable. Drainage or marsupialization may have to be done when adhesions, size and location prevent the ideal treatment. Partial excision leaves a draining sinus, which frequently becomes infected. The statistics prove the desirability of complete extirpation, showing a cure in 71 per cent of the cases. Hedblom [7] gave the mortality for 99 patients in all surgical hands as 16.1 per cent.

## SUMMARY

To summarize, the history, with pathologic report, roentgenograms and photomicrographs, of a case of teratoma of the mediastinum in a 7 month old child is presented. There were details in the history and physical findings which have been found frequently in other cases of intrathoracic dermoid. The diagnosis was made with the aid of roentgenograms and an examination of the aspirated fluid from the chest. Complete removal of the tumor offers the best chance for cure.

Dr. Milton Rabson, of the department of pathology, described the gross and microscopic material and assisted in preparing the photomicrographs of the sections.

11. Eloesser, L., in discussion on Harrington,[6] p. 71.

# Progress in Pediatrics

## CIRCULATORY COLLAPSE IN DIPHTHERIA

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By way of introduction I should, perhaps, outline the field covered by the science of pharmacology and the relation that the subject bears to the practice of medicine. One of the youngest of the preclinical sciences, pharmacology was born in Europe in the latter half of the last century and later was transported to America, the first department of pharmacology in this country being established in Ann Arbor, Mich., in 1889 by Dr. John J. Abel. In 1893 Dr. Abel was called to Johns Hopkins University to establish a similar laboratory at that institution and was succeeded at Michigan by Dr. Arthur R. Cushny, who remained as head of the department until he was called to University College, London, England, in April 1905. It would be impossible to estimate the influence of these two men on the history of pharmacology in this university. No other pharmacologic laboratory in this country has started under such advantageous circumstances, and the influence of the names and work of these men has permeated all the members of the department in the years which have followed.

As its name indicates, pharmacology concerns itself with the study of the action of drugs. It is therefore as Pomet, chief druggist to Louis XIV, wrote in 1712, a "Study so agreeable and so exalted in its own Nature that it has been the Pursuit of the finest Genius's in all Ages: Several Princes have applied themselves to it with a great deal of satisfaction to their own minds and Improvement to the Publick."

Previous to the birth of pharmacology the knowledge of the action of drugs and of their value in the treatment of disease was gained in a more or less haphazard fashion. Substances of all sorts derived from vegetable, animal and mineral sources were administered to the sick and if improvement followed were given the credit and in turn given to subsequent patients exhibiting like symptoms. This is so-called empirical practice.

In this manner the values of certain drugs were learned, and as a result of this human experimentation such remedies as quinine, mercury, digitalis and salicylic acid came into general use. With the advent of

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The Henry Russell Lecture of the University of Michigan for 1937.

the modern era of scientific medicine, efforts were made to learn the action of drugs in the animal body and to apply the knowledge so acquired to their rational use in the treatment of disease. As a result, there has been a complete revolution in the development of therapeutics. For the last half century not a single drug of importance, barring perhaps the liver preparations, has been introduced into practice except through the laboratory. No one would think today of administering to a patient a drug of which the action and the toxicity had not previously been carefully studied on the lower animals. Hence there are all the modern local antiseptics, all the local anesthetics, hypnotics and antipyretics, and all the antisyphilitic remedies, products of cooperation between chemist, pharmacologist and clinician. The criticism is voiced at times that these studies have been carried out only on healthy animals and that, not unlikely, there is a great gap between a healthy dog and a sick man. While this criticism is not valid and can easily be answered, efforts have been made in recent times to produce in animals, so far as is possible, diseases similar to those which afflict the human subject. In certain cases this can be done, while in others it is impossible, as in many instances animals are not susceptible to the same diseases which affect man. However, certain of the organisms which affect man will grow in the animal body and produce changes comparable to those of the human disease. In other instances the organisms may be grown in the test tube and produce toxins the action of which can be studied in the laboratory by methods similar to those employed with common drugs. In the past few years some of these bacterial poisons have been so studied, and they have yielded information not only of scientific interest but also of importance in the treatment of the sick.

The toxin which I have studied most intensively is that formed by the organism of diphtheria. This poison is especially favorable for study, in that it can be injected into lower animals, in which it will produce pathologic changes closely analogous to those seen in the disease in man. When this organism is attacked it must be remembered that today the cause of death in diphtheria is not suffocation from obstruction of the air passages, as it was fifty years ago. The use of antitoxin has largely changed this. Now the main cause of death is to be found in the failure of the circulation, which occurs usually at about the height of the disease, perhaps between its fifth and its twelfth day. The patient may have severe local manifestations of the disease and show a picture of profound intoxication. So far as the circulatory system is concerned, the pulse is weak and rapid, the heart sounds are loud but labored, and enlargement of the liver indicates a beginning circulatory failure. The blood pressure, which has been nearly normal, begins to fall and the patient is dead within an hour or so. It is this type of case which I have especially studied—one in which death is usually described as due to heart

failure but in which it should perhaps be more properly ascribed to a circulatory collapse. There is another group of cases, in which death may come much later—even when the patient is well on in convalescence—but in those cases the cause of the fatality is different from that in those grouped as "early cases," and in such cases the condition calls for a different type of treatment.

Treatment in the early cases has been by so-called cardiac stimulants, such as digitalis, strychnine and camphor, and it was a study of the value of such remedies [1] which first occupied the attention of my associates and me in the laboratory, as it was possible to produce in animals circulatory conditions analogous to those seen in the human subject. It was found early in the work that in the primary stage of the circulatory collapse, before the blood pressure has fallen greatly, digitalis will act in a normal manner, increasing the strength of the contractions of the heart. In the severer forms of collapse, however, when the pressure has fallen to a low point, the drug has little value and, indeed, has proved to be positively dangerous. Even in the early stages in which the drug has been found effective, the heart is unusually susceptible to its action, and doses which are entirely safe for the normal animal are highly dangerous to the diphtheritic subject. An unusual susceptibility of the human diphtheritic patient to digitalis was pointed out earlier by McCullough,[2] a pediatrician of St. Louis, who warned against the use of the drug in this condition. Our results entirely justified his warning. However, a year or two later, Gold,[3] of New York, denied that there is any synergistic relation between the action of toxin and that of the drug unless the animal is moribund. Still later Myers,[4] of Cambridge, England, published results seeming to prove that the administration of digitalis to animals would protect them to a considerable degree against fatal doses of diphtheria toxin. These two reports being so radically opposed to our findings of increased susceptibility, my associates and I [5] extended our study of the subject, using exact methods for comparing the toxicity of the drug in normal and in diphtheritic animals. These results confirmed the earlier findings and showed that one-half the normal lethal dose of digitalis is fatal to a diphtheritic animal. Whereas for normal animals 110 mg. of digitalis per kilogram of body weight is the fatal dose, for diphtheritic animals the fatal dose

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1. Edmunds, C. W., and Cooper, R. G.: Action of Cardiac Stimulants in Circulatory Failure Due to Diphtheria, J. A. M. A. **85**:1798 (Dec. 5) 1925.

2. McCullough, H.: South. M. J. **14**:110, 1921.

3. Gold, H.: Tolerance to Digitalis in Experimental Diphtheria, J. A. M. A. **87**:2047 (Dec. 18) 1926.

4. Myers, G. N.: J. Pharmacol. & Exper. Therap. **44**:191, 1932.

5. Edmunds, C. W.; Smith, R. G., and Moyer, C. A.: J. Pharmacol. & Exper. Therap., to be published.

is 80 mg. if the action of the heart is regular or 60 mg. if the cardiac action, owing to the toxin, is irregular. Here, therefore, is a clear demonstration of greatly increased susceptibility in these animals. These clinical and experimental results have been explained recently by pathologic studies carried out in different laboratories.[6] The studies showed that digitalis itself when given in large doses or over a prolonged period produces lesions in the cardiac muscle which resemble closely those resulting from diphtheria toxin; the lesions are most serious when they affect those special fibers which conduct the impulses from auricle to ventricle and thus produce an arrhythmia of the heart. The results obtained by my associates and me [7] agreed with these in showing that animals with irregular heart beats succumb to doses of digitalis approximately one-half those fatal to normal animals.

Among other drugs studied, one or two deserve special mention. Strychnine and camphor, both of which are popularly known as cardiac stimulants, were found to have no value in this condition. Even today, however, statements advocating the use of these and other stimulants to the central nervous system for this condition of circulatory failure may still be found in textbooks and in some of the original articles on the treatment of diphtheria, in spite of the overwhelming experimental and clinical evidence that the cause of the circulatory collapse is to be sought elsewhere than in the central nervous system and that drugs such as camphor and its allies are useless. Epinephrine furnished perhaps the greatest surprise. Derived from the adrenal glands, this substance is perhaps the most active circulatory stimulant in existence. Injected intravenously into normal animals, a minute fraction of a milligram will profoundly stimulate the heart and contract the blood vessels, thus producing a marked increase in blood pressure. In the diphtheritic dog, however, the activity of the drug is tremendously reduced. In the earlier stages of the disease, before the blood pressure has fallen markedly, it may approximate more or less closely its normal activity. In the more serious stages of the circulatory collapse, however, doses of epinephrine perhaps one hundred times normal will have little or no effect.

This failure of epinephrine to act furnished a clue to one of the causes of the circulatory failure. The physiologic or anatomic structure in both the heart and the blood vessels which is stimulated by the epinephrine undergoes in diphtheria a certain degree of depression or paralysis, so that it no longer is able to transmit impulses to the heart and the blood vessels, whether these impulses come from the central

6. Büchner, F.: Arch. f. exper. Path. u. Pharmakol. **176**:59, 1934.

7. Edmunds, C. W., and Johnston, F. D.: Circulatory Collapse in Diphtheria, J. A. M. A. **90**:441 (Feb. 11) 1928.

nervous system through the vasomotor nerves or from the chemical agent, epinephrine. Thus, the nervous impulses which continually pass from the vasomotor center to the blood vessels are no longer able to reach them, and the vessels, released from the tonic impulses which ordinarily keep them contracted, relax, and the blood pressure falls. The blood, therefore, pours more and more into the dilated vessels and thus tends to accumulate in the large vascular areas in the abdomen and not to return to the heart in sufficient amounts to enable the organ to maintain the normal blood pressure. Naturally, the heart, already diseased, suffers first from the low pressure; all the organs in the body, including the brain, follow in turn, and the condition, unless rapidly relieved, is likely to lead to a fatal termination. The condition might well be compared to surgical shock. It is, indeed, a toxic shock.

The obvious aim of the treatment is to restore the circulation. If it is impossible to effect recovery of the paralyzed blood vessels, at least the heart must be furnished with sufficient fluid to maintain an adequate supply to the various organs of the body.

For this purpose my associates and I injected physiologic solution of sodium chloride warmed to body temperature into the blood vessels, but while the blood pressure was raised during the period of injection, it fell as soon as the administration was stopped, owing to the rapid passage of the fluid from the vessels into the lymph spaces. The same difficulty was encountered in the use of solution of sodium chloride in surgical shock. A solution of acacia, which, owing to its colloidal nature, remains in the vessels for a longer time, was used, but it, too, was unsatisfactory, although the pressure was maintained better with it than with the saline solution. Finally, a 10 per cent solution of dextrose which has been warmed to 40 C. was injected slowly into the blood stream. Its administration was followed immediately by a remarkable improvement in the condition of the heart and in the blood pressure. The heart became stronger; the pulse was increased, and the blood pressure rose rapidly, the improvement lasting for a considerable time, depending on conditions and on the amount of dextrose solution injected. When, after a time, the pressure began to fall once more, it was possible to restore it promptly by another injection of dextrose. The effect of the dextrose was truly life saving. While it would not restore a heart which had stopped beating, if the solution could be introduced into the veins while the heart was still contracting, it never failed to revive the heart. The use of this solution, of course, is in a large degree an emergency measure—a temporary expedient—but it is one which may tide a person or an animal over a crisis and perhaps give time for other remedial agents to act or for the natural recuperative powers of the body to prevail.

The question naturally arises as to how the dextrose solution acts to produce its favorable results. It is manifest that in the first place the solution furnishes fluid to increase the volume of the circulatory blood and, owing to the character of the dextrose molecule, retains the water in which it is dissolved within the vessels and does not allow it to pass out into the lymph spaces. Then, too, it furnishes, through its oxidation, an important source of energy to the heart and to the tissues in general. This action is of great importance, as in recent years various workers [8] have shown that in the earlier stages of diphtheria there is a marked decrease of sugar (dextrose) in the blood, which indicates a serious interference with carbohydrate metabolism. The main source of energy for bodily activity is the carbohydrate of the food. This after absorption is taken to the liver in the form of dextrose and stored there as glycogen, which is then drawn on as needed, and reconverted into dextrose, in which form it can be utilized by the body.

In diphtheria, owing to the toxin, the action of the liver is impaired to such a degree that the glycogen either is not stored or is broken down, so that in experimental animals postmortem examination may show little glycogen in the heart, the liver or the muscles. This disappearance of glycogen in the disease is reflected in the low content of sugar in the blood. This disturbance in sugar metabolism is doubtless associated with other nutritional disturbances in the tissues, and it is most probable that the degenerative changes in the heart and the muscles are due, in part at least, to these nutritional disturbances. With these facts established, it is entirely logical to conclude that at least one of the explanations of the favorable effects of the administration of dextrose lies in its ability to correct the deficiency in blood sugar and thus to prevent some of the pathologic changes which would otherwise occur in the tissues of the heart and of the body generally.

Further studies on carbohydrate metabolism have shown that, while dextrose administered to normal animals is quickly removed from the blood, in diphtheritic subjects an abnormally high sugar content persists for a considerable time after the administration. Some workers, notably Schwentker and Noel,[9] of Baltimore, have expressed the thought that this condition denotes a toxic action on the pancreas, which interferes with the formation of insulin, and they therefore have advocated the giving of insulin, in order to aid the body in disposing of the dextrose. This advice was based, of course, on a somewhat similar excess of dextrose in the blood of patients with diabetes. As a result of the

8. Lereboullet, P.; Marie, P. L., and Leprat, L.: Paris méd. **12**:417 (Nov. 4) 1922.

9. Schwentker, F. F., and Noel, W. W.: Bull. Johns Hopkins Hosp. **45**:276, 1929; **46**:259 and 359, 1930.

work of these investigators, a number of clinicians have combined the use of insulin with that of dextrose and, as I shall point out later, have reported favorable results. However, it is difficult to say whether the insulin is necessary in treating this condition or whether it is superfluous. The arguments for its administration are not impressive, as they postulate injury not only to the pancreas but to the thyroid and the adrenal glands. It is possible that the beneficial effects of the dextrose are gained in spite of the insulin and not because of it. This view is the more plausible because many clinicians do not use insulin with the dextrose and yet have favorable results. An important contribution to the subject was furnished by Begg,[10] of the North Eastern Hospital of the London County Council Infectious Service. In his study 124 patients suffering from severe diphtheria were given dextrose, but to each alternate patient insulin was given as well. From a statistical standpoint the results in the two groups of patients were identical, although actually the number of deaths was slightly higher in the group receiving insulin—15, as compared with 13. In any case, the essential substance is certainly the dextrose. Harries, the superintendent of the hospital where Begg's work was done, said of the value of dextrose therapy in toxic diphtheria: "There can be no two opinions amongst those who have observed its effects in a long series of cases."

In this discussion of the part that the blood vessels play in the lowering of the blood pressure, it must not be supposed that the condition of the heart is overlooked—far from it. It is well known that the heart undergoes profound pathologic changes in diphtheria. One of the most exhaustive studies which has been made on the subject was that of the late Professor Warthin.[11] The hearts of experimental animals also were studied by him and more recently by Professor Weller, and both reported the presence of essentially the same pathologic changes in animals as are seen in human beings suffering from diphtheria. It goes without saying that a heart that has undergone the pathologic changes typical of diphtheria cannot function normally, and in the end, if these changes are sufficiently marked, they are bound to be the determining factor and cause death. However, even though the animals showed cardiac changes comparable to those seen in human subjects, when the dextrose solution was supplied, their hearts promptly revived and were amply able to maintain a respectable blood pressure, thus demonstrating considerable reserve power.

To illustrate the strikingly beneficial effects of the dextrose solution, the record of one dog may be given: This animal, as the result of two injections of toxin, was dying. It was comatose and at the commence-

10. Begg, N. D., and Harries, E. H. R.: Lancet **1**:480 (March 2) 1935.

11. Warthin, A. S.: J. Infect. Dis. **35**:32, 1924.

ment of the experiment stopped breathing. Artificial respiration was quickly started, and the heart continued to beat feebly, but the carotid artery was practically empty, and the blood pressure was 10 mm. of mercury. Warmed dextrose solution was quickly injected, and immediate improvement in the heart and the blood pressure followed. Various other remedies were used, such as solution of acacia, epinephrine, digitalis and strychnine, but without any favorable results. Solution of posterior pituitary caused temporary improvement, but dextrose was by far the most effective agent, the blood pressure under its influence finally reaching 90 mm. of mercury.

This was a clear demonstration of the ability of a badly diseased heart to maintain a good pressure, as the pathologic report in this instance showed "marked hemorrhages under the epicardium and the endocardium, chronic myocarditis, atrophy of the heart muscle, Zenker's necrosis of the heart muscle, and fatty degenerative infiltration of the papillary muscles." The other organs showed changes seen only in a malignant type of diphtheria.

An important point, which was manifest in all the animals studied and clearly shown in the case just detailed, is that the early use of the dextrose is important. Not only is the reaction of the animal much better in the early stage of the disease than when it is moribund, but if part of the beneficial effect of the dextrose is due to the avoidance of extreme pathologic alterations, then the earlier the dextrose is used the better the results will be. This fact is of great importance in the clinical application of this form of treatment.

Still other structures which must be considered in any study dealing with circulatory disorders due to diphtheria are the adrenal glands. These small organs are situated on either side of the spinal column directly above the kidneys. From the medullary portion of the glands the active substance known as epinephrine is derived. Pharmacologically, epinephrine, as I have said earlier, is perhaps the most active circulatory stimulant known, but its importance in the normal life of the individual animal is still a matter of dispute. According to one view, it is secreted continuously into the blood stream, while, according to another, it is only of value in emergencies, such as those due to great physical strain. In the normal dog epinephrine is present in the glands to the extent of about 0.1 per cent. In the laboratory my associates and I [12] have studied the adrenal glands of many diphtheritic dogs and found, as have others, that the glands show a great diminution in epinephrine content, some possessing even as little as 20 per cent of the normal amount. But a similar poverty of epinephrine is found in many other conditions associated with acute infections and in certain cachectic diseases, such as tuberculosis. Hence, it is not specific for diphtheria and may have

12. Edmunds, C. W., and Johnston, F. D.: Am. Heart J. **4**:16, 1928.

nothing to do with the circulatory collapse of the disease. Also, the diminution of epinephrine in disease is generally brought about through a slow and gradual process, while the circulatory collapse considered here is comparatively sudden. On the other hand, it may well be questioned whether a stock of epinephrine in the body from 75 to 85 per cent below normal may not play some part in the life expectancy of the animal.

Before proceeding to a brief review of the clinical application of the work which has been carried on in the pharmacologic laboratory, it would seem well to bring together in a short summary the changes which appear to be responsible for the early deaths in cases of diphtheria. It is impossible to give them in order of importance, and certainly there is no complete agreement among authorities as to which are the most important. It may be proper, therefore, to place the condition of the heart first, as the changes which that organ undergoes in diphtheria have been studied most intensively and there cannot be the slightest doubt that it plays a most important rôle in determining the final outcome. Other organs and tissues are also affected, and among these must be placed the blood vessels, which undergo a progressive and relatively rapid paralysis, leading to a sudden fall in blood pressure and an accumulation of blood in the abdominal area. This leads to impoverishment of the remainder of the body, including the heart and the brain, and results in sudden death. Together with these changes, there is a marked disturbance in sugar metabolism, leading to a diminished sugar content of the blood, which in turn is responsible, at least in part, for further pathologic changes in important organs.

As has been shown, the intravenous injection of dextrose is most useful in treating the experimental emergency, and it will be interesting to see whether the suggestion emanating from the laboratory can be carried over to the clinic, and if so with what success. Unfortunately, it is too often the case that a procedure which has good results in the laboratory, where all the factors can be carefully controlled, may not be so successful when applied under the difficult conditions of bedside practice.

One of the most prominent writers on diphtheria in the last two or three years is Dr. Paul Kiss,[13] of the University Children's Clinic of Budapest. Dr. Kiss says that, as a result of the work of my associates and me, he tried blood transfusion and the injection of dextrose in two children with malignant diphtheria, one aged 6 and the other 8 years. The first child died on the twelfth day of the disease, and the second child, on the fifteenth. The results were certainly not favorable, and Kiss concluded that the cause of death in diphtheria is to be sought

13. Kiss, P.: Arch. f. Kinderh. **101**:84, 1934.

in the pathologic changes in the heart and that filling the peripheral vessels is without value.

After the clinical histories of these two cases have been studied, it can hardly be said that the dextrose treatment was given a fair trial. In the first case, on the sixth day, 20 cc. of a 40 per cent solution was given; on the seventh day, 40 cc.; on the eighth day, none; on the ninth day, 40 cc.; on the tenth day, 20 cc., and on the eleventh and the twelfth day, none, in spite of the fact that the child was taking no nourishment and that, as the history states, the "pulse was empty." In all, only 120 cc. was given in the course of six days, and on three days none was given. In the second case, the child was given 40 cc. of a 40 per cent solution on the fifth day; on the sixth and the seventh day, none; on the eighth day, 100 cc. of a 10 per cent solution; on the ninth and the tenth day, none; on the eleventh and the twelfth day, 20 cc. of a 40 per cent solution; on the thirteenth day, none, and on the fourteenth day, 20 cc. of a 40 per cent solution. On the fifteenth day the child died. The children, it is true, received fairly large transfusions of blood, and certain drugs, such as camphor and ephedrine, were administered, but it does seem that the failures in these two cases can hardly be charged against dextrose, as certainly insufficient dextrose was given (120 cc. in the first case and the equivalent of only 105 cc. of a 40 per cent solution in the second case). It was given as a concentrated solution, thus supplying little fluid. Also, on several days it was omitted entirely.

I have discussed earlier the use of insulin with dextrose, the theory being that insulin will aid the tissues in the utilization of the dextrose.

One of the first persons to employ the treatment combining dextrose and insulin was Kostýal,[14] of the Children's Clinic of Tisza-István University, Debrecen, Hungary. He instituted treatment with dextrose in 121 cases, adding the insulin in only those of the most severe involvement. He reported that the results were good; the general condition and the appetite of the children improved, and the mortality, which in an earlier period had reached 32 per cent, when the dextrose was being supplied fell to 12 per cent. Excluding patients who were moribund when admitted to the hospital, the mortality was 6.9 per cent and 5.4 per cent, respectively, in succeeding six month periods.

Woodcock,[15] of the Leeds (England) City Hospital, employed a similar form of treatment in 25 cases of severe diphtheria in which he said he ordinarily would have expected a mortality of 100 per cent. Eight patients recovered. Woodcock remarked that after the use of dextrose one gets an "impression of relief from discomfort and distress and that sometimes this relief is very marked."

14. Kostýal, L.: Monatschr. f. Kinderh. **48**:162, 1930.
15. Woodcock, H. E. de C.: Lancet **2**:894 (Oct. 22) 1932.

Benn, Hughes and Alstead,[16] of the Birmingham (England) City Hospital, reported a mortality of 22.5 per cent in 89 cases, as compared with a 35.9 per cent mortality for a group of 131 patients treated previously without dextrose and insulin.

In these three studies, insulin was given, while in this country dextrose alone seems to have been almost exclusively employed. Within a short time after the appearance of the first paper in which my associate and I advocated the use of dextrose, Dr. J. A. Toomey,[17] associate professor of pediatrics, Western Reserve University School of Medicine, Cleveland, reported at the meeting of the Central States Pediatric Society the results of the use of dextrose in 46 patients. In all the cases reported the disease was severe, and the glands of the neck were so enlarged as to form a "collar." He said in previous years he would have expected a 100 per cent mortality, whereas of this group of 46 patients, 24, or 52 per cent, lived. In reporting this 50 per cent decrease in mortality, he said that after the injection of dextrose the blood pressure rises; "the collapsed veins, which frequently are present, become filled again; the general cyanosis of the patient becomes modified in a short time; the cheek loses its pasty color and the skin, its clammy feel; a healthy sweat breaks out, and adults often say that they feel better."

Darrow and Yannet,[18] of the department of pediatrics of Yale University School of Medicine and the New Haven Hospital, in their studies described a definite injury to the blood vessels, as well as to the liver and other organs. They reported that they employed repeated injections of dextrose and that large amounts of fluid may be injected even if cardiac decompensation is present. It has been suggested by some that the giving of additional fluid by vein may overburden a diseased heart, but Darrow and Yannet said that this is not to be feared. They reported that one of their patients who recovered received no fluids by other than the venous route for eleven days. A 5 year old child received 785 Gm. of dextrose during its illness, on the tenth day receiving 1,500 cc. of solution intravenously.

Friedemann,[19] of the Rudolph Vircow Hospital in Berlin, in a recent extensive review of the circulatory disturbance of diphtheria, agreed that its cause lies in a paralysis of the blood vessels and that the more severe the disease may be, the more severe will be the vascular

16. Benn, E. C.; Hughes, E., and Alstead, S.: Lancet **1**:281 (Feb. 6) 1932.

17. Toomey, J. A.: Clinical Observations with Injections of Dextrose in Diphtheria, Am. J. Dis. Child. **35**:722 (April) 1928.

18. Darrow, D. C., and Yannet, H.: Physiologic Disturbances in Diphtheritic Intoxication with a Note on Therapy, Am. J. Dis. Child. **46**:671 (Sept.) 1933; Symptomatic Therapy in Malignant Diphtheria, ibid. **49**:60 (Jan.) 1935.

19. Friedemann, U.: Deutsche med. Wchnschr. **58**:1644 (Oct. 14) 1932.

injury. He added that there is little value in giving stimulants to the central nervous system and that the essential factor in treatment is the administration of sufficient fluid. Mautner,[20] of Vienna, in discussing the treatment of malignant diphtheria, recommended the use of dextrose rather than the ordinary cardiac drugs, as the dextrose improves the nutrition of the heart and fills the blood vessels. The blood being in the abdominal organs, the heart practically runs dry.

Beck,[21] of Karlsruhe, Germany, also studied the low sugar content of the blood and pointed out that the cardiac changes occur at this time. He expressed the belief that the decrease in the sugar content comes first, and is followed by the poverty of glycogen in the liver. Finally injury to the cardiac muscle follows, as a result of the disturbance of carbohydrate metabolism. He therefore recommended giving dextrose plus insulin and cited cases in which the cardiac disturbances disappeared completely when dextrose was administered. He said that, while he could show a few electrocardiographic curves, "what I cannot demonstrate graphically is the always renewed puzzling improvement in the general condition of the sick child." Knauer,[22] Bonn, Germany, reported use of 8 per cent solutions of dextrose every three hours in diphtheria and said: "The action is without doubt good." Bottner [23] said that in the recent (1935) epidemic in Königsberg, Germany, he employed repeated injections of dextrose, as the treatment of the circulatory weakness is important.

The most detailed and extensive report on the use of dextrose solutions in diphtheria comes from the Municipal Contagious Disease Hospital in Chicago, where, as a result of work performed by my associates and me, this method of treatment was adopted under the supervision of the medical superintendent, Dr. A. L. Hoyne.[24] The administration of the dextrose solution gave such favorable results immediately that its use was extended, and, instead of being given only in cases of severe diphtheria with actual or impending circulatory failure, it is now used much more widely and several injections are given daily. It is given to all patients who have been ill for three days without administration of antitoxin; to those with marked involvement of the cervical glands; to those with renal complications, and to all those in whom the condition is malignant. In cases in these classifications a 10 per cent solution of dextrose is given at once—500 cc. for a child and 1,000 cc. for an adult, and like amounts are administered daily for eight days. One woman

20. Mautner, H.: Wien. klin. Wchnschr. **45**:1387 (Nov. 4) 1932.

21. Beck, O.: Monatschr. f. Kinderh. **62**:74, 1934.

22. Knauer, H., in discussion on Beck,[21] p. 81.

23. Bottner, A.: Deutsche med. Wchnschr. **61**:839 (May 24) 1935.

24. Hoyne, A. L., and Welford, N. T.: J. Pediat. **5**:642, 1934. Hoyne, A. L.: Am. J. M. Sc. **191**:271, 1936.

received 13,365 cc. (1,365 Gm.) of a 10 per cent solution of dextrose in thirty-seven days. During the year 225 patients with diphtheria were admitted to the hospital, in 83 of whom the condition was classed as malignant diphtheria; the accepted mortality in such cases is about 60 per cent. After exclusion of two of the patients who died almost immediately after their admission and who could not, therefore, be considered in judging the efficiency of the dextrose, the mortality among the remaining 81 patients, instead of being from 50 to 60 per cent, was 9.8 per cent. Many of these patients, Hoyne said, were in "the condition of impending death; with a waxy pallor of the skin, almost pulseless, unable to speak. Following the injection their color would improve, they would return to consciousness and even attempt to raise themselves to a sitting position." He added that "in some of the patients there was a spectacular recovery apparently attributable to glucose therapy." He gave the clinical history of a 3 year old boy, which I will repeat in an abbreviated form, as it illustrates better than any description I can give the therapeutic effect of the dextrose.

The child was admitted to the hospital on the seventh day after onset of the disease, suffering from a most malignant type of diphtheria. The details of his symptoms I will omit, merely adding that he was in an extremely toxic condition, semicomatose and with a blood pressure of 60 systolic and 0 diastolic. As circulatory failure was imminent, repeated injections of epinephrine were given, without any benefit resulting. A 10 per cent solution of dextrose was then given. On the next day the blood pressure was 60 systolic and 50 diastolic; the pulsation of the heart was scarcely audible and markedly irregular, its rate being 168. The boy appeared waxy and was comatose. He was given 100 cc. of the dextrose solution, after which he opened his eyes, smiled and asked intelligent questions for the first time since he entered the hospital. Further injections of dextrose were followed by a stronger pulse, less irregularity of the heart beat and a return of pinkness to the cheeks. On the fourteenth day the patient suffered from paralysis of the larynx and the throat, so that he could not speak or swallow. This was followed in two days by paralysis of the neck and the back. His heart, however, continued to improve, so that dextrose was discontinued on the seventh day, and the boy was discharged on the fifty-second day, entirely recovered except for an occasional irregular beat of the heart.

This case is interesting and instructive, and Hoyne said he felt that the child would surely have died had it not been for the dextrose. In Hoyne's first series of cases, in which he used dextrose only after cardiac complications had arisen, the death rate was lowered by only 10 per cent. However, when he began the administration of dextrose earlier in the course of the disease and gave it repeatedly, the rate of mortality was lowered from 60 per cent to less than 10 per cent. He expressed the belief that by the early use of dextrose myocarditis can often be prevented.

Finally, it would seem that the experiences of Hoyne and the other authorities mentioned would offset the unfavorable impressions which Kiss gained from the results in his two cases.

However, the clinical use of dextrose in diphtheria cannot be said to be definitely standardized as yet. Clinical results and laboratory findings indicate that a 10 per cent solution should be given early, before symptoms of cardiac disturbance or circulatory failure appear, the administration to be repeated as often as necessary. The circulatory system is thus directly aided and the heart protected in some degree from the injury which it would undoubtedly suffer owing to the disturbances in carbohydrate metabolism. Probably in the average case the protective action on the heart would be the more important rôle of the dextrose but in a circulatory emergency in which signs of impending death are present the effect is so immediate and so striking that a direct action on the circulation is the only explanation possible. However, aside from the theoretical reasoning, the fact remains that, in the words of Beck, of Karlsruhe, Germany, "these severely sick children that ordinarily would be lost can in many cases be helped, and that is the main point."

# Abstracts from Current Literature

## Biochemistry; Bacteriology, and Pathology

IMMUNOLOGIC SPECIFICITY OF STAPHYLOCOCCI. L. A. JULIANELLE, J. Bact. **33**:49 (Jan.) 1937.

With increasing interest in immunology as related to staphylococcic infections Julianelle has made studies concerning the specificity of staphylococci. He feels that there are at least two immunologic types, which are definable not by agglutination but by precipitation of the respective carbohydrate extracted from the organisms. One type, A, is composed of strains isolated from pathogenic conditions, while the other type, B, comprises strains from nonpathogenic sources. The specific carbohydrates are differentiated chemically, by optical rotation and by the simple sugars resulting from hydrolytic cleavage. The specificity of the carbohydrates is proportional to the degree of hydrolysis.

Skin reactions elicited by the carbohydrates are due almost entirely to type A, the reactions occurring in few normal infants and children but reaching a maximum frequency of from 65 to 70 per cent in normal adults. In these instances no precipitins accompany the skin reactivity. Patients recovering from infection also exhibit skin reactivity to type A carbohydrate, but only those suffering from generalized or severe prolonged infection elaborate specific precipitins.

STOESSER, Minneapolis.

BACTERICIDAL ACTION OF HUMAN SERUM ON HEMOLYTIC STREPTOCOCCI. W. S. TILLETT, J. Exper. Med. **65**:147 (Jan.) 1937.

The results presented concern the destructive action of serum from patients who are acutely ill on hemolytic streptococci.

Serum obtained from twenty-five patients at the time of acute active infections was in every instance bactericidal for hemolytic streptococci. Among the diseases represented in the group were infections due to the pneumococcus, the hemolytic streptococcus, the staphylococcus, the meningococcus, the tubercle bacillus and malarial parasites; the etiology of the other diseases represented was uncertain, or some may have been due to mixed infections.

In serum taken from the same group soon after recovery or after marked improvement, the streptococcidal property was absent or greatly diminished.

By comparative tests made with serum from twenty healthy adults, the streptococcidal action was not demonstrable.

KNICKERBOCKER, Dallas, Texas.

A NATURAL HEMOLYSIN FROM THE RAT PRODUCING NUCLEAR LYSIS OF CHICKEN ERYTHROCYTES. D. WEINMAN, J. Immunol. **32**:1 (Jan.) 1937.

A natural hemolysin for chicken erythrocytes was found in the blood of rats. This substance differed from hemolysins previously described in that it caused lysis of the nucleus as well as of the cytoplasm, with liberation of hemoglobin. A detailed description of the morphologic changes occurring in cells under the influence of this hemolytic and karyolytic substance is given.

FOTHERGILL, Boston.

STUDIES ON BARBITURATES: XX. THE ALLEGED ANTICOMPLEMENTARY AND ANTICOAGULANT ACTION OF BARBITURATES. M. MOLLARI, W. A. RANDALL and T. KOPPANYI, J. Immunol. **32**:35 (Jan.) 1937.

The authors reinvestigated the previously published claims of others that phenobarbital completely inhibits complement, prevents coagulation of the plasma of citrated blood when heated to from 50 to 60 C. and inhibits the coagulation of whole blood.

This investigation yielded the following results: Large amounts of soluble barbital U. S. P. (sodium barbital) and soluble phenobarbital U. S. P. (sodium phenobarbital) inhibited complement hemolysis and prevented coagulation of citrated plasma; small amounts had no effect. Barbital and phenobarbital had no effect even in saturated solution. It was found that sodium carbonate was as effective as the sodium salts of the aforementioned drugs when the hydrogen ion concentration of the mixture was the same as that in the drug mixture. It was concluded that the inhibition of complement and the prevention of coagulation were due to the alkalinity of the medium.

FOTHERGILL, Boston.

A STUDY OF THE ORIGIN OF NATURALLY OCCURRING IMMUNE BODIES FOR PNEUMOCOCCI IN INFANTS. W. D. SUTLIFF and J. A. V. DAVIES, J. Immunol. **32**:43 (Jan.) 1937.

The gradual development of the pneumococcidal action of whole blood was studied in a group of nine infants. Repeated cultures were made from the nasopharynx in order to determine the relationship between the bacterial flora of the upper respiratory tract and the development of bactericidal action. During a period of five months the development of the killing action of the blood for type II pneumococci was observed in three infants. A similar action against type III pneumococci occurred in one infant. No specific relationship was found in any infant between the strain of pneumococcus present in the nasopharynx and the pneumococcidal action that subsequently developed.

FOTHERGILL, Boston.

STUDIES ON THE FATE OF LIVING BACTERIA INTRODUCED INTO THE UPPER RESPIRATORY TRACT OF NORMAL AND INTRANASALLY VACCINATED RABBITS. P. R. CANNON and T. E. WALSH, J. Immunol. **32**:49 (Jan.) 1937.

Cannon and Walsh studied the distribution of bacteria in the respiratory tracts of rabbits and guinea-pigs when the bacteria were instilled intranasally in small amounts of fluid. Nonvirulent staphylococci passed quickly and directly into the lungs by way of the trachea and bronchi. Virulent pneumococci did not pass directly through the epithelium of the upper respiratory tracts of normal rabbits. They were aspirated into the lungs and thence entered the blood stream. Intranasal vaccination with formaldehyde-killed pneumococci did not prevent aspiration of living organisms into the lungs following instillation of these organisms into the nostrils. Such vaccination, however, inhibited growth of the organisms in the lung and restricted their entrance into the blood stream. The importance of gravity and of respiratory suction was emphasized.

The authors point out that the results of their experiments emphasize "the hazard of purulent secretions in the nostrils of infants and young children in the course of upper respiratory infections, and point to the danger inherent in the use of oily nasal drops in the treatment of such infections."

FOTHERGILL, Boston.

TOXIC POTENTIALITIES OF CONTINUED ADMINISTRATION OF CHLORATE FOR BLOOD AND TISSUES. A. P. RICHARDSON, J. Pharmacol. & Exper. Therap. **59**:101 (Jan.) 1937.

In view of the widespread use of potassium chlorate in certain dentifrices, (41.6 per cent has been found in one preparation) and the known toxicity of large quantities of the drug, Richardson investigated its toxicity in pigeons and cats.

Fatality was associated with "widespread sloughing of the kidney epithelium and marked periportal fatty degeneration in the liver." Methemoglobinemia occurred only shortly before death or post mortem. Doses of the chlorate necessary to produce similar toxicity and death in man would be many times that required in the cats used, but it should be recalled that 30 Gm. has caused fatality in man. The work would not seem to argue against the relatively small doses of

chlorate used in the treatment of ulcerative stomatitis in children, i. e., from 0.6 to 1 Gm. daily for a few days only. This dosage the reviewer believes to be useful and harmless. Richardson rightly condemns the use of chlorates in dentifrices as lacking a rational basis, and particularly in view of the possible toxic effects from swallowing considerable quantities of the dentifrice. PILCHER, Cleveland.

IMMUNIZING ACTIVITY OF CERTAIN CHEMICAL FRACTIONS ISOLATED FROM HEMOLYTIC STREPTOCOCCI. T. C. STAMP and E. B. HENDRY, Lancet **1**:257 (Jan. 30) 1937.

From strains of hemolytic streptococci belonging to groups A and C fractions have been isolated capable of inducing active immunity in mice. The active fraction from strains of group C is soluble in dilute acids but insoluble in ammonia and is probably a protein. The active fraction from strains of group A resembles that from strains of group C in being acid soluble, but it is inactivated by ammonia. It also appears to be a protein. LANGMANN, New York.

REDUCIBLE BY-PRODUCT OF STOKVIS IN THE BLOOD AND URINE OF NORMAL MEN. L. A. HULST, Nederl. tijdschr. v. geneesk. **81**:313 (Jan. 23) 1937.

In the blood as well as in the urine of normal persons the "reducible accessory product" of Stokvis (the "pentdyopent" of Bingold, 1934) is present. This is surmised to be an oxidation product of bilirubin, which is always present under physiologic conditions. It is not known where this oxidation takes place.

VAN CREVELD, Amsterdam, Netherlands.

METHOD FOR DETERMINATION OF CALCIUM IN SERUM. P. MULLER, Nederl. tijdschr. v. geneesk. **81**:352 (Jan. 23) 1937.

The calcium of serum was determined by the direct method of de Waard, by the indirect method of Halverson and Bergeim and by first ashing the serum according to Neumann. The direct method gives good results. The indirect method gives values that are too high, possibly through contamination with amino-acids.

VAN CREVELD, Amsterdam, Netherlands.

## Metabolism; Infant Feeding; Milk and Other Foods

SOME CLINICAL OBSERVATIONS ON FEEDING INFANTS WHOLE MILK, GELATINIZED MILK AND ACIDIFIED MILK: A PRELIMINARY REPORT. C. L. JOSLIN, Arch. Pediat. **54**:20 (Jan.) 1937.

Three groups of fifty children were fed on whole milk, gelatinized milk and acidified milk, respectively. The components, milk, water and carbohydrate, in all formulas varied in direct proportion to the weight of the child. The gelatinized formulas contained 1 or 2 per cent gelatin, and the acidified milk formulas, 3 drops of lactic acid to each ounce (29.5 cc.) of whole milk. In addition to infants whose feeding was normal each group included infants who suffered from minor digestive disturbances, such as vomiting, anorexia and constipation.

*Rate of Gain During Treatment*

| | Average Number of Ounces per Week | Average Number of Months of Treatment |
|---|---|---|
| Cow's milk | 4.7 | 6 |
| Gelatinized milk | 5.7 | 4½ |
| Acidified milk | 5.3 | 5 |

*Results of Various Feedings on Digestive Disturbances*

| | Infants with Vomiting | | | | Infants with Anorexia | | | Infants with Constipation | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Treated | Cured | Improved | Not Improved | Treated | Improved | Not Improved | Treated | Cured | Improved | Not Improved |
| Cow's milk | 14 | 6 | .. | 8 | 2 | .. | 2 | 17 | 7 | .. | 10 |
| Gelatinized milk | 22 | 14 | 7 | 1 | 3 | 3 | .. | 13 | 11 | 2 | .. |
| Acidified milk | 11 | 8 | .. | 3 | 1 | .. | 1 | 16 | 10 | 4 | 2 |

Infants fed on gelatinized and acidified formulas enjoyed a better rate of gain in weight per week and had a reduction in the incidence of digestive disorders. Attention is called to the lower incidence of respiratory infections in the group of infants fed on gelatinized milk. Nine of this group as compared with twenty-one on cow's milk and twenty-four on acidified milk had respiratory infections.

ORR, Buffalo.

A SPECIAL HYDRATING SOLUTION IN INFANT FEEDING. F. S. SMYTH and S. HURWITZ, Arch. Pediat. **54**:71 (Feb.) 1937.

Newly born full term infants were given an alkaline sugar formula as a prelacteal feeding. The authors state that in their experience an alkaline hydrating solution as a prelacteal feeding is not as efficacious as a buffered lactic acid mixture.

ORR, Buffalo.

STUDIES IN MINERAL METABOLISM: CALCIUM AND THE KIDNEY; EXPERIMENTAL. B. CHOWN, M. LEE and J. TEAL, Canad. M. A. J. **36**:7 (Jan.) 1937.

In a previous paper the authors described the types and sites of early calcium deposits in rats treated by injection of parathyroid extract and some methods by which the kidney rids itself of calcium. The present paper deals with the parenchymal and interstitial changes which they have observed. Three types of gross lesions have been produced: (1) cystic dilatation of tubules without pelvic change; (2) irregular pelvic dilatation with more or less cystic dilatation of tubules; (3) chronic focal nephritis with a mildly granular condition of the surface of the kidney and very slight cystic changes.

It appears reasonably certain that the pathologic changes described depend on deposition of insoluble calcium salts, but how these act, and why in one rat simple focal nephritis develops, in another polycystic disease and in a third great pelvic irregularity, the authors do not know. They believe that these experiments lend weight to suggestions previously made that human pyelonephritis and polycystic kidney have in some cases a fault in mineral metabolism as their primary cause.

MOORE, Omaha.

IRON METABOLISM OF NORMAL YOUNG WOMEN DURING CONSECUTIVE MENSTRUAL CYCLES. R. M. LEVERTON and L. J. ROBERTS, J. Nutrition **13**:65 (Jan.) 1937.

Four normal young college women were the subjects for the study. Two were studied for approximately four months and two for five months. The menstrual periods in all subjects were regular and normal according to subjective criteria of amount and duration of flow. The diets contained only the minimal iron requirement of from 10 to 15 mg. per day. The results suggest that the low values for hemoglobin which are accepted for women because of the drain due to small periodic losses in the menses may instead be due to the use of diets low in iron.

MUNNS, Winnetka, Ill.

MILK CURD—ITS MECHANISM AND MODIFICATION. I. N. KUGELMASS, Arch. Dis. Childhood **12**:25 (Feb.) 1937.

The curd tension of milk diminishes rapidly with dilution. Fifty per cent dilution delimits soft curd milk. Milk modifiers diminish the curd tension as diluents of the clotting constituents. Heating alters the curd tension. A rise in the temperature of milk to about 40 C. actually increases curd tension, while subsequent heating diminishes it, with a maximum at body heat. The time of heating at various temperatures likewise modifies the character of the curd, the diminution in curd tension being more marked the higher the temperature of heating. The curd tension is a function of the hydrogen ion concentration of milk, with a maximum at about $p_H$ 6. On both the acid and the alkaline side of this maximum there is marked diminution in curd tension. Additions of milk modifiers displace this maximum to a flattened zone extending from about $p_H$ 5.5 to 6.5. Each acid produces a characteristic curd at the same $p_H$ in the following order: hydrochloric, phosphoric, acetic, lactic and citric. Hydrochloric acid produces the softest curd and citric acid the firmest. Colloidal milk modifiers diminish the curd tension progressively in the following order: sugars, barley, banana, gelatin. Milk modifiers alter the volume of the clot. Heat, dilution, acidification, alkalinization and colloids produce swelling of the clot while additions of the clotting constituents, casein, calcium and rennet, produce a shrinking of the clot. Swelling of the clot is conducive to soft curd formation and shrinking to hard curd.

KELLY, Milwaukee.

FOOD AND NUTRITION. E. P. CATHCART, Brit. M. J. **1**:435 (Feb. 27) 1937.

This is an abridgment of a lecture known as the Sir Charles Hastings Lecture, given under the auspices of the British Medical Association. This lecture does not lend itself to abstracting. It is a timely, logical and intelligent discussion in brief of various phases of malnutrition and undernutrition with reference to socio-economic strata of society and with special emphasis on the question of the financial budget.

ROYSTER, University, Va.

SIGNIFICANCE OF THE SO-CALLED ACETONEMIC CRISIS IN HYPOGLYCEMIC COMA. J. CATHALA, S. B. BRISKAS and M. LORAIN, Arch. de méd. d. enf. **40**:18 (Jan.) 1937.

The authors report in full detail the case of a boy aged 4 who entered a medical clinic in profound coma with a provisional diagnosis of poisoning on account of the unusual brusqueness of onset. Examination showed complete absence of the tendon reflexes, with the pupils normal. There was a faint odor of acetone in the breath, and the urine was free from sugar and albumin. The reactions of Gérardt and Le Gall were positive; the blood sugar was found to be 32 mg. per hundred cubic centimeters. Within two hours, without the use of sugar or bicarbonate, the coma disappeared, but the child remained inert and complained of headache. The evolution of the glycemia and the reactions of acidosis were followed for a week, while the symptoms gradually disappeared. The sugar content fluctuated between 25 and 70 mg., and the $p_H$ varied from 7.29, with an alkaline reserve of 52, to 7.25, with a reserve of 42.

Since infections and all forms of intoxication could be excluded, and a more careful investigation revealed that the boy had sustained several similar, though milder, attacks, the authors concluded that the invasion was autotoxic in origin and represented a grave assault on the humoral and acid-base equilibrium as well as on the metabolism of sugar. It is interesting to note that without any treatment and in spite of the amplitude of the deviation the organism could reestablish through its own forces complete compensation.

AMESSE, Denver.

ADDITION OF POWDERED LEGUMES TO INFANTS' FOOD. F. RUBINI, Lattante **8**:21 (Jan.) 1937.

Blood studies (hemoglobin estimation, red blood cell count, white blood cell count, differential count) were made on twelve infants before and after the addition of powdered legume to their milk feedings. The patients were all over 6 months of age. Some were breast fed, some artificially fed, and some were being given mixed feedings.

After three months there was noticed a definite rise in the hemoglobin. There was also found an increase in lymphocytes at the expense of the neutrophilic cells. The improvement is attributed to the mineral and vitamin content of the legumes.

HIGGINS, Boston.

THE TOTAL ORGANIC ACIDITY AND LACTIC ACID OF THE BLOOD SERUM IN FEEDING CASES. C. CAMMARELLA, Pediatria **45**:15 (Jan.) 1937.

Cammarella has proposed to examine the relation between the total organic acidity and the lactic acid content of the blood serum in cases in which feeding is a problem. For the determination of organic acids he used the method of Csapó; for that of lactic acid, the method of Mendel and Goldscheider with slight modifications. In cases in which normal feeding prevailed he obtained values for organic acids corresponding to a range of between 9.10 and 13.85 cc. of a solution of tenth-normal acid per hundred cubic centimeters of serum.

For lactic acid he does not give a definite average value, because the value is subject to a state of rest or irritability of the infant before and during the removal of blood (from the longitudinal sinus). During rest the content does not differ from that of the older children having an average value of 20.5 mg. per hundred cubic centimeters, varying as it does between 16 and 25 mg. The value in the normal infant can rise to 50 mg. with crying or active movements. In pathologic conditions, as in laryngospasm, he found an increase in lactic acid, while the total acidity was normal because of diminution in the remaining organic acids; in bronchopneumonia the total organic acids greatly increased, while the lactic acid varied in cases in which toxicity was prominent; in such cases he noted marked and constant increase of the total organic acidity, while in typical cases with acute onset the lactic acid was likewise increased; in other cases it was almost normal.

He concludes that there is no relationship between total organic acidity and lactic acid, stating that the intermediary metabolism can in certain cases affect and in other cases preserve the exchange of carbohydrates, of which lactic acid is one of the important compounds; the extent of the metabolism disturbance is related to the degree and extension of hepatic dysfunction.

PALMIERI, Brooklyn.

EFFECT OF ULTRAVIOLET RAYS ON THE PHOSPHORUS AND DEXTROSE OF THE BLOOD. G. PAVAN and C. MORO, Riv. di clin. pediat. **35**:1 (Jan.) 1937.

Exposure of normal (nonrachitic) children to small doses of ultraviolet rays led to an increase in the phosphate and a diminution in the sugar of the blood. With stronger irradiation, however, a reverse effect was noticed in that the phosphorus diminished and the sugar increased. In vitro, exposure of blood serum to ultraviolet rays gave an increase of inorganic phosphorus. Similar results were obtained by irradiation of rabbits.

HIGGINS, Boston.

TREATMENT OF INTOXICATION IN INFANCY. C. INCLAN, Arch. de med. inf. **6**:120 (March) 1937.

From 1922 to 1924 the method used was hypodermoclysis and intraperitoneal injection of dextrose. The mortality was 90 per cent. From 1925 to 1928 blood transfusions were used, and the mortality was 70 per cent. From 1929 to 1932 lactate-Ringer solution (as devised by Dr. A. F. Hartmann) was used, and the mortality was 60 per cent. From 1933 to date the treatment has consisted in withholding all food and using venoclysis as described by Schick and Karelitz. The mortality has been 14 per cent.

SANFORD, Chicago.

ADVANTAGES OF A MODERATELY HIGH ALTITUDE FOR CHILDHOOD DISEASES. F. HAMBURGER, Wien. klin. Wchnschr. **50**:17 (Jan. 8) 1937.

Hamburger notes that attempts to explain the effect of different types of climate have been only partially successful. Physicians are satisfied that climatic variations in different regions affect health, even though they are unable to explain the mechanism. There can be no doubt that moderately high altitude (from 600 to 1,000 meters) often influences various diseases, expedites recovery and prevents recurrences. The proportionate rôles of sunlight (especially in the formation of vitamin D by the agency of the ultraviolet rays), of sharp differences in temperature during the day and night and of fresh air are not fully understood.

In addition to the effect of light and air, the psychic effect of climatic therapy is especially noteworthy. The author ascribes considerable significance to increased muscle tonus and improved appetite, whereby the resistance of the child is increased. One is forced to conclude that many diseases develop or take a severe course merely because of unfavorable light and air or unfavorable effects of certain environments on the psyche.

Tuberculosis in almost all its forms can be favorably influenced by moderately high altitude. A notable exception is the markedly progressive form. A stay in the mountains is especially important for children who are recovering or convalescing from tuberculosis, as well as for children who have recently acquired an infection. In the first two years following an initial tuberculous infection, it should be urged that the child spend four weeks in the country in the winter time, preferably in the mountains.

Moderately high altitude is also indicated for children who are suffering from nose and throat infections, infections of the upper respiratory tract, asthma, and subacute and chronic swellings of the glands of the neck. It must be noted that results of climatic therapy are often slow, and the treatment may have to be continued many months. The author does not believe that a stay in the mountains is contraindicated for hysterical or neuropathic children. Care must be taken as to those who accompany the child. If the mother or any other member of the family has an irritating effect on the child, some other person should be chosen to accompany the child.

The author believes that moderately high altitude is contraindicated only in rheumatic illnesses, such as acute rheumatic fever and chorea. For all other frequent illnesses there is no contraindication.

ABT, Chicago.

DYSTROPHIES IN INFANTS. M. A. ABBOUD, J. Egyptian M. A. **20**:17 (Jan.) 1937.

There is nothing unusual about this article except the use of antiquated terminology, which made it difficult for the reviewer to understand always just what Abboud meant.

MULHERIN, Augusta, Ga.

STUDIES ON GAS METABOLISM IN CHILDREN: IV. THE BASAL METABOLISM IN VERY YOUNG CHILDREN. M. DE BRUIN, Nederl. tijdschr. v. geneesk. **81**:884 (Feb. 27) 1937.

The basal metabolic rate of thirty-one boys and thirty-eight girls with body weight ranging from 6.5 to 14 Kg. has been determined by means of the apparatus of Dusser de Barenne and Burger. It was thus possible to extend the standard curve that had been composed for older children to earlier age groups. In the majority of the children the influence of sleep on the basal metabolic rate could be examined. A marked decrease was constantly found, the extent of which varied in the individual cases, generally amounting to from 10 to 20 per cent of the level before sleep.

VAN CREVELD, Amsterdam, Netherlands.

## Vitamins; Avitaminoses

EFFECT OF VITAMIN D ON INTESTINAL ATONY OF RICKETS. L. YODER, Am. J. Digest. Dis. & Nutrition **3**:828 (Jan.) 1937.

Rachitic rats were fed viosterol for six days, while controls from the same litter were not fed the vitamin. After the six days lamp black, 1 per cent, was incorporated in the ration of both the deficient and the vitamin-treated rats. The time of the first feeding of the carbon ration was noted and thereafter the time of the first appearance of black feces.

The data showed that rats fed a minimal amount of vitamin D had increased motility of the intestine. The lamp black appeared in the stools of the rats fed viosterol from 25 to 30 per cent quicker than in the rats not fed viosterol.

MORRISON, Savannah, Ga.

EFFECT OF VITAMIN D ON INTESTINAL IRON REDUCTION. L. YODER, Am. J. Digest. Dis. & Nutrition **3**:829 (Jan.) 1937.

When irradiated ergosterol was administered to rachitic rats in a quantity sufficient to produce a continuous line of calcification these rats showed a decreased amount of fecal reduced iron. Unirradiated ergosterol had no effect. Therefore, this is apparently characteristic of vitamin D.

MORRISON, Savannah, Ga.

THE PRESENT EVALUATION OF VITAMIN $B_1$ THERAPY. M. G. VORHAUS, Am. J. Digest. Dis. & Nutrition **3**:915 (Feb.) 1937.

This article is an attempt to evaluate vitamin B therapy. The article is lengthy and lends itself poorly to abstracting. Needless to say the subject is still vague and still in the process of emerging from the status of an experimental problem to that of an accepted clinical concept.

An interesting fact brought out very clearly in this article is that the second most frequent cause of infant mortality in China, the Philippines and adjacent countries is infantile beriberi. The vast majority of these infants are born of mothers who have beriberi.

MORRISON, Savannah, Ga.

FURTHER STUDIES ON INTOXICATION WITH VITAMIN D. I. E. STECK, H. DEUTSCH, C. I. REED and H. C. STRUCK, Ann. Int. Med. **10**:951 (Jan.) 1937.

The effects of massive doses of vitamin D in animals and in human subjects are discussed. The administration of 20,000 units per kilogram of body weight per day for indefinite periods did not result in intoxication. Hypervitaminosis D produced cell injury followed by deposits of calcium. When administration of vitamin D was discontinued, repair followed. Intoxication for short periods did not result in permanent injury of tissue.

READING, Galveston, Texas.

COMPARATIVE ANTIRACHITIC EFFECTIVENESS OF VIOSTEROL, COD LIVER OIL AND PERCOMORPH LIVER OIL. J. M. LEWIS, J. Pediat. **10**:155 (Feb.) 1937.

Because of the divergence of results regarding the relative effectiveness of cod liver oil and viosterol in infants an investigation of this problem was carried out, and at the same time the antirachitic value of percomorph liver oil was studied. Both the prophylactic and the curative value of these three substances were studied in 365 infants.

Each one of these antirachitic agents was given to groups of infants at the respective rates of 135, 435 and 870 U. S. P. XI units daily throughout the winter months. At the end of the winter the incidence of rickets among the infants was determined by roentgenologic examination of their wrists. The results of the prophylactic study showed no significant difference in the effectiveness of these agents at the level of units employed. One infant in each of four groups (50 infants

receiving 135 units of viosterol daily, 58 infants receiving 435 units of this oil, 50 infants receiving 135 units of cod liver oil and 51 infants receiving 435 units of this oil daily) showed development of rickets. One infant in a group of 46 infants receiving percomorph liver oil, 135 units daily, showed rickets. Infants receiving from 435 to 870 units showed no evidence of rickets.

Fourteen rachitic infants from 3 to 8½ months of age were tested with viosterol, percomorph liver oil, cod liver oil and irradiated cholesterol. A daily dose of 435 units of cod liver oil, percomorph liver oil and irradiated cholesterol brought about good healing in 2, 4 and 3 rachitic infants, respectively, whereas the same number of units of viosterol failed to cause satisfactory healing in 2 infants. Lewis concludes that this study seems to indicate that rat unit for rat unit vitamin D from an animal source is more effective in the treatment of infantile rickets than vitamin D of plant origin.

RAUH, Cincinnati.

USE OF VITAMINS IN CHILDREN'S DIETS. C. A. ALDRICH, M. Clin. North America **21**:63 (Jan.) 1937.

While practically all the known vitamins seem to be necessary in order that the general growth of the body may proceed, it seems unlikely that they supply necessary building stones in this process. It appears more probable that they act as catalysts in the chemical reactions of growth, and that growth is not quantitatively dependent on the dosage of the vitamins. Together with the property of promoting growth in general each vitamin seems to have a specific influence on the histologic development and function of specific tissues. The lesions resulting from a diet deficient in a vitamin are therefore characteristic for the vitamin, and to a certain extent the severity of the changes varies with the degree and duration of the deficiency. It is also probable that the functions of many of the endocrine glands are related to specific vitamin changes, but knowledge of these relationships is as yet inadequate.

Following an eminently sane review of the established facts concerning the various vitamins and their uses, Aldrich admits the importance of these substances for normal growth and for life itself. He questions, however, the necessity of routine administration of all of them to children in the form of concentrates. All except vitamin D are available in ordinary diets. Modern methods of processing and preparing foods doubtless lead to a deficiency of these substances in the diets of both adults and children. Teaching children to eat a wide variety of foods as little changed from their natural state as possible seems a rational method of correcting this deficiency.

EUGENE SMITH, Ogden, Utah.

CALCIUM AND VITAMIN D IN METABOLIC PROCESSES. S. A. CLARK, M. Rec. **145**:72 (Jan. 20) 1937.

The scientific facts connected with residence in the semitropics do not receive the attention they deserve. Normal metabolism with calcium as a factor is largely dependent on the presence of vitamin D. Vitamin D is made available in two ways, namely, by being taken as a food adjunct and second through irradiation. The foods rich in vitamin D are egg yolk, butter fat and fish oils. Solar rays stimulate through the skin the formation of vitamin D. Exposure of the skin to solar rays increases vital resistance, and the increased vital resistance engendered and induced by residence in the semitropics lessens incidence of disease.

When the factors of longevity in the semitropics are considered, all evidence seems to be in favor of those who appreciate the sunlight enough to live where it is available.

WILLIAMSON, New Orleans.

SCURVY IN TWINS WITH REPORT OF CASES. F. CLARKE and C. W. BYRNES, Nebraska M. J. **22**:21 (Jan.) 1937.

Twins, James and Jerome, aged 7 months, were brought into the hospital on account of failure to take feedings and gain in weight or strength. The former

over a period of five weeks; the latter, three weeks. The babies were listless and cried and screamed when handled during periods of five and two weeks, respectively. There was swelling of the knees and legs, with pain on motion and tenderness during periods of five and two weeks, respectively. During a period of four months small amounts of cooked tomato juice were given about twice a week. There were no changes in the gums. After giving orange juice for ten days the irritability, listlessness, edema and pain suddenly disappeared, and in four weeks they were discharged as cured.

HAMILTON, Omaha.

VITAMIN C AND THE FORMATION OF INTERCELLULAR MATERIAL. S. B. WOLBACH, New England J. Med. **215**:1158 (Dec. 17) 1936.

Vitamin C (cevitamic acid) is necessary for the formation of all intercellular substances having collagen as their basis. Its absence prevents therefore the formation of the matrices of white fibrous tissue, bone, cartilage and dentin. The consequences of its absence are most apparent in growing animals and in the repair of lesions of these tissues. The deficiency does not prevent multiplication of the cells of each type of tissue, but the cells assume a common morphologic character, approximately that of embryonic connective tissue, and histologic appearances indicate that a liquid material is produced in lieu of the normal matrix.

Because cell division continues in absolute vitamin C deficiency and therefore the synthesis of proteins, the speculations of a morphologist are along the lines of attributing to cevitamic acid a late rôle in the formation of collagen.

GENGENBACH, Denver.

PROGRESS IN EARLY RECOGNITION OF VITAMIN DEFICIENCY STATES. K. D. BLACKFAN, New England J. Med. **215**:1159 (Dec. 17) 1936.

Quantitative chemical tests are at hand, ready for clinical application, whereby the concentration of vitamins A, $B_1$, C and D can be measured with a certain degree of confidence. For vitamin A, the antimony trichloride test is the best suited clinically. Carr and Price found that antimony trichloride produces a blue color with vitamin A. The average value of the vitamin in man on an adequate diet as determined by the Lovibond tintometer is 40 blue units or approximately 0.05 mg. of vitamin A, per hundred cubic centimeters of serum.

Peters has shown that in vitamin $B_1$ deficiency there is a defect in the oxidation of certain carbohydrate intermediates in nerve tissue—in particular, pyruvic acid. Vitamin $B_1$ is the factor that serves to promote its oxidative removal. Pyruvates have been found in the blood of patients with beriberi in China, and the blood of experimentally depleted animals contains pyruvic acid in relatively large amounts. Feeding vitamin $B_1$ to the depleted animals causes pyruvic acid to disappear and brings about restoration to full health.

The chemical test for vitamin C is made with the dye indophenol blue, which forms a colorless compound with cevitamic acid. This test is widely used in the analysis of urine and tissue for cevitamic acid. Oral administration of a series of test doses of 200 mg. of cevitamic acid provides valuable information as to the state of vitamin C nutrition, as a surplus of cevitamic acid is not excreted until the storage in the tissues is adequate. After saturation has been reached, 75 per cent of a 200 mg. dose is excreted in the urine within eight hours after ingestion.

Before rickets is recognizable clinically, determinations of the calcium and phosphorus in the blood serum indicate that optimal amounts of vitamin D are not available. If the serum phosphorus is less than 3 and the calcium phosphorus product is less than 40 mg. per hundred cubic centimeters, there is moderate or severe rickets. It should be emphasized that the figures for calcium and phosphorus require evaluation from the standpoint of activity of growth and level of serum protein.

It has been claimed that the most sensitive test for detecting active or current rickets is found in measuring the phosphatase of the blood. In the beginning of the disease the phosphatase is increased, and it does not return to normal until healing is complete.

GENGENBACH, Denver.

RELATION OF AVITAMINOSIS TO ORAL PATHOLOGY. P. R. HOWE, New England J. Med. **215**:1163 (Dec. 17) 1936.

Evidence has been disclosed to indicate that dental disasters of today are largely due to deficiencies of minerals and vitamins in the body. There is some evidence in studies of the vitamins to support the finding in diffraction studies, in that unsuspected changes occur in the organic substance of teeth and bones in such a condition as rickets. The same pathologic response to deficiency of vitamin A, C or D and the same recovery therefrom when the deficient animal is furnished with the missing factor are seen in the teeth as elsewhere.

It is the hope of present day research workers that medical men will work to build good dental conditions by advising proper nutrition in prenatal and early postnatal periods, so far as this is understood, and that dentists will regard dental disturbance not as an isolated phenomenon but as a result of general physiologic conditions.

GENGENBACH, Denver.

PRECISE EVALUATION OF ULTRAVIOLET THERAPY IN EXPERIMENTAL RICKETS. J. W. M. BUNKER and R. S. HARRIS, New England J. Med. **216**:165 (Jan. 28) 1937.

Depilated rachitic rats were irradiated with measured quantities of monochromatic ultraviolet rays to determine the number of ergs required to produce a "narrow continuous line of calcification." Ultraviolet radiation from the mercury vapor arc in quartz, passed through a quartz monochromater, was measured by photochemical and physical methods.

The principal mercury lines between 2,537 and 3,025 angstroms, inclusive, were demonstrated to have antirachitic properties. Lines immediately above and below this region were inactive. To produce rachitic healing equivalent to that produced by 3 U. S. P. units of vitamin D, the following energies per rat were required:

| Angstroms | Ergs |
|---|---|
| 2,537 | 775,000 |
| 2,652 | 660,000 |
| 2,804 | 600,000 |
| 2,967 | 420,000 |
| 3,025 | 900,000 |

These differences are probably due in part to differences in absorption of the various wavelengths by the skin. They are likely due in part to the absorption spectrum of the provitamin. On a quantum basis the antirachitic effectiveness of the various wavelengths is not the same.

GENGENBACH, Denver.

BISULPHITE BINDING SUBSTANCES IN THE BLOOD IN HEALTH AND IN DISEASE, PARTICULARLY VITAMIN $B_1$ DEFICIENCY. R. W. WILKINS, F. H. L. TAYLOR and S. WEIIS, Proc. Soc. Exper. Biol. & Med. **35**:584 (Jan.) 1937.

Bisulfite-binding substances have been reported increased in blood in vitamin $B_1$ deficiencies, both in experimental animals and in patients with "wet beriberi." Samples of blood from 30 healthy controls and 110 patients with various clinical disorders were examined. In normal blood the values for bisulfite-binding substances averaged 4.74 mg. (range, 3.66 to 5.75). An increase over these values was found in decompensated heart disease, unregulated diabetes, vascular nephritis, lobar pneumonia and certain other febrile diseases, untreated chronic alcoholism with $B_1$ deficiency, terminal uremia, pancreatitis and pernicious vomiting, as well as with factors such as acidosis, ketosis, anoxemia, "toxemia" and uremia. In certain cases of vitamin $B_1$ deficiency and of diabetes the increase in bisulfite-binding substances could not be related to the aforementioned factors. In both these conditions, in a few of the cases studied, abnormal amounts of pyruvic acid were found in the urine. There is a question as to whether or not the increase of the bisulfite-binding substances in these conditions represents an increase also of the pyruvic acid of the blood. The authors have not found the increase in

these substances in the blood of aid in diagnosing vitamin $B_1$ deficiency, which seldom occurs without possible complication by one or more of the other diseases in which there may be an elevation of the level of these substances.

HANSEN, Minneapolis.

THE DETERIORATION OF VITAMIN D IN AQUEOUS SOLUTIONS. D. H. SHELLING, Proc. Soc. Exper. Biol. & Med. **35**:660 (Jan.) 1937.

Clinical studies with rachitic children revealed that vitamin D in emulsified oily solutions added to milk lost in healing properties fairly rapidly. A 5 per cent emulsion of 250D viosterol with milk, or 500 international units per gram, kept on ice lost in potency as follows: After three weeks, it assayed 280 units; after 6 weeks, 125 units; after 6 months, less than 40 units. The containers were opened from time to time, and no effort was made to exclude air. Kept in sealed vials, the emulsion showed only slight loss of potency. Loss of potency in canned evaporated milk was practically nil.

HANSEN, Minneapolis.

AN EXCRETORY TEST FOR VITAMIN C DEFICIENCY AND SUBNUTRITION. E. P. RALLI, G. J. FRIEDMAN and M. KASLOW, Proc. Soc. Exper. Biol. & Med. **36**:52 (Feb.) 1937.

The excretion of vitamin C in the urine after an intravenous injection of 100 mg. of cevitamic acid was followed in a group of twelve normal subjects on diets adequate in vitamin C, in three subjects on diets low in vitamin C and in thirteen persons with scurvy. The method of Birch, Harris and Ray (*Biochem. J.* **27**:590, 1933) was used for determining the excretion of vitamin C. Three hour and twenty-one hour excretion periods were used. Forty per cent of the injected vitamin was excreted in three hours in normal subjects, 11 per cent in persons suffering from subnutrition and 2.5 per cent in the group with scurvy. This supports the view that the three hour urinary excretion of vitamin C following an intravenous dose of cevitamic acid will serve as an index of vitamin C deficiency or subnutrition.

HANSEN, Minneapolis.

SIGNIFICANCE OF PLASMA PHOSPHATASE IN THE DIAGNOSIS AND PROGNOSIS OF RICKETS. N. MORRIS, M. M. STEVENSON, O. D. PEDEN and J. M. D. SMALL, Arch. Dis. Childhood **12**:45 (Feb.) 1937.

The plasma phosphatase was estimated in a group of 506 infants and children below the age of 2 years. In 84.1 per cent. of infants with clinical or roentgen evidence of rickets the plasma phosphatase was increased above normal limits. It is suggested that a rise in plasma phosphatase is an earlier manifestation of the rachitic state than that provided by ordinary clinical or roentgenographic examination. A rough parallelism was observed between the height of the phosphatase and the severity of the rachitic process, but it is pointed out that the level of the phosphatase cannot be taken as an index of the severity in the individual patient. A moderate degree of correlation was observed between the rise in phosphatase and the fall in phosphorus and in the calcium-phosphorus product, especially the latter, and it would appear that of the three an increase in plasma phosphatase is the most delicate test of the rachitic state, although it would be unwise to use alteration in phosphatase alone as conclusive evidence of the presence or absence of rickets.

In untreated active rickets the plasma phosphatase continues to rise. Administration of vitamin D prevents this rise and in two to three weeks causes a fall. The rate of fall depends on the dosage of vitamin D, being much more rapid with large amounts. On ordinary therapeutic doses normal limits may not be reached for over three months. The significance of high plasma phosphatase is discussed, and it is suggested that the phosphatase is increased whenever the supply of calcium is unable to meet the demand of the bone cells as a result of defective intake of minerals or of vitamin D.

KELLY, Milwaukee.

THE VITAMIN C CONTENT OF COW'S MILK AND COW'S MILK MIXTURES. O. MEULEMANS and J. H. DE HAAS, Indian J. Pediat. **4**:1 (Jan.) 1937.

Using a previously described method for the quantitative determination of vitamin C, the authors found the vitamin C content of fairly fresh cow's milk as distributed in Batavia to be ± 1.5 mg. per hundred cubic centimeters and that of milk subjected to protracted transportation to be no more than 0.6 mg., as compared with from 4 to 7 mg. in mother's milk. They also found that kitchen boiling hardly affects the vitamin C content of cow's milk, if at all.

GONCE, Madison, Wis.

QUANTITY OF VITAMIN C IN MOTHER'S MILK AS AFFECTED BY A CHANGE OF CLIMATE. F. RUBINI, Lattante **8**:7 (Jan.) 1937.

The vitamin C content of the milk of twenty mothers was determined before and at the end of a forty day sojourn at the seashore. There was an increase in sixteen cases, practically no change in three, and a decrease in one case. The median value was increased from 2.95 to 3.90 mg. per hundred cubic centimeters.

HIGGINS, Boston.

TREATMENT OF RICKETS. M. BARBONE, Lattante **8**:26 (Jan.) 1937.

Observations were made on twelve rachitic children treated with a commercial product that contains phosphorus, calcium, magnesium, parathyroid gland and vitamin D. The blood chemistry (phosphorus, calcium, magnesium, potassium) showed cure of the rickets.

HIGGINS, Boston.

EFFECT OF THE ANTISCORBUTIC VITAMIN ON THE OXALIC ACID CONTENT OF THE BLOOD. A. LEONE, Lattante **8**:55 (Feb.) 1937.

The blood of normal guinea-pigs contains approximately 2 mg. of oxalic acid per hundred cubic centimeters. In experimentally produced scurvy the oxalic acid was found to have disappeared. The giving of cevitamic acid to normal guinea-pigs increases the oxalic acid in the blood.

HIGGINS, Boston.

RICKETS IN HAVANA. G. CARDELLE, R. PEREIRAS and L. PASCUAL, Arch. de med. inf. **6**:15 (March) 1937.

Rickets is rare in Havana. Only 2 per cent of the infant population have it, in a mild form. The principal factor is deficiency of vitamin D, with inadequate diet and lack of sunshine as accessory factors. Chronic infections, intoxications and syphilis predispose to it. Craniotabes is rare, but in one case it was seen associated with rickets. The natural treatment in Cuba should be heliotherapy.

SANFORD, Chicago.

FREQUENCY OF RICKETS IN BRAZIL. M. GARCIA, O. P. CAMPOS and O. DE ALMEIDA SILVA, Arch. de pediat., Rio de Janeiro **9**:7 (Oct.) 1936.

In the last few years articles by Xavier, de Barros and Baptista have remarked on the infrequency of rickets in Brazil. Recently in this journal Guimaraes reported a case of rickets as a rarity. The authors state that in ten months in the Hospital Jesus they have observed seven cases of typical rickets, two being in Negroes. There are some excellent roentgenograms and photomicrographs to substantiate this diagnosis. [Rickets is presumed to be practically unknown in Brazil. There is no question of the diagnosis in these cases; so estimates of its frequency in tropical countries may need revision. Abstractor.]

SANFORD, Chicago.

OIL OF WHEAT GERM IN PRACTICAL PEDIATRICS AND OBSTETRICS. M. FLAMINI, Med. inf. **8**:48 (Feb.) 1937.

Flamini extracted the fat from the wheat germ and made observations following its ingestion by rats, by pregnant women, by lactating mothers and by infants. This oil is rich in vitamins A, D and E. Rats to which it had been given produced more frequent litters and larger young. Pregnant women who had taken the oil gave birth to bigger babies. Lactating mothers receiving from 20 to 30 drops of this oil daily showed an increase in secretion of milk. In artificially fed children, the use of 10 drops of the oil daily improved the general health and vigor.

HIGGINS, Boston.

VITAMIN THERAPY IN DAILY PRACTICE. E. WILLE, München. med. Wchnschr. **84**:534 (April 2) 1937.

Wille found patients in his private practice with a variety of complaints in whom he failed to find any abnormality on physical examination or by laboratory tests. He tried vitamin therapy in these cases. Patients complaining of a variety of symptoms, such as headache, fatigue, difficulty in swallowing, rheumatic pains or nerve pains, have been improved or cured by taking vitamin B or C. He suggests that rheumatism is a deficiency of vitamins B and C.

BRAHDY, Mount Vernon, N. Y.

BLOOD SUGAR IN INFANTILE BERIBERI, BREAST MILK INTOXICATION AND CARBOHYDRATE DYSPEPSIA. S. KOHDA, Acta pædiat. japon. **43**:73 (Jan.) 1937.

In infantile beriberi the blood sugar is within normal limits but is below normal in breast milk intoxication and in carbohydrate dyspepsia of the beriberi type.

KATO, Chicago.

CAPILLARY BLOOD PRESSURE IN INFANTILE BERIBERI. I. KOBAYASHI, Acta pædiat. japon. **43**:93 (Jan.) 1937.

By Kylin's method Kobayashi measured the capillary blood pressure in infants with beriberi, using normal infants as controls. He reports the following results: (1) In normal infants the capillary pressure is 72 mm. of water at three months and gradually increases during the first year, with an average of 84 mm. of water. (2) In infants with beriberi capillary pressure is greatly elevated in direct proportion to the severity of the cardiac damage, being on the average from 90 to 100 mm. of water. (3) The administration of vitamin B preparations in infantile beriberi causes the pressure to fall to the normal level. (4) The rise in capillary pressure resulting from artificially induced passive congestion is similar to that seen in infantile beriberi, leading to the inference that passive hyperemia may directly cause the high capillary blood pressure in this disease. (5) Unless they manifest severe symptoms of avitaminosis B, the capillary blood pressure in mothers nursing infants suffering from infantile beriberi is usually normal. (6) Injection of pitressin (betahypophamine) causes a significant fall of capillary blood pressure in infantile beriberi, suggesting its possible use in the treatment of circulatory disturbance in beriberi.

KATO, Chicago.

ALLERGY AND BLOOD SERUM IRRADIATED WITH ULTRAVIOLET RAYS. M. MURAYAMA, J. Orient. Med. **26**:727 (April) 1937.

In previous studies Murayama pointed out the beneficial effects from the use of irradiated blood serum in the treatment of such allergic diseases as urticaria, Quincke's edema, infantile eczema and others. The present study aims at determining the effect of irradiation on the desensitizing power of the serum. The following observations are recorded: 1. The complements and antibodies in sensitized guinea-pig serum appear to return to their antesensitization state on injec-

tion of irradiated autoserum. 2. The speed of hemagglutination and the blood picture resulting from sensitization with egg-white in guinea-pigs appear to revert to their original state on repeated injections of irradiated autoserum. 3. The injection of irradiated blood serums from man, horse, pig and sheep into normal guinea-pigs produces certain definite symptoms, such as elevation of temperature, tremor, urination and defecation. 4. While normal serums of guinea-pig and horse as well as egg-white have no effect on the uterine musculature, the irradiated serums and egg-white cause contraction of the virgin uterus, the action closely simulating that of histamine. 5. The minimal lethal dose of horse serum is found to be from 0.00005 to 0.0001 cc. for the guinea-pig sensitized three weeks previously by the minimal sensitizing dose of horse serum (0.0000115 cc.). 6. The sensitized guinea-pig can be desensitized by repeated intradermal injections of irradiated autoserum. 7. The therapeutic effect of irradiated serum on allergic diseases appears to be due to its desensitizing power as well as to the suppressing tendency arising from the elaboration of a histamine-like substance following irradiation.

KATO, Chicago.

## Hygiene; Growth and Nutrition; Public Health

A PROPER DIETARY AS A PUBLIC HEALTH MEASURE (RELATION TO INFANCY AND CHILDHOOD). E. J. WYNKOOP, New York State J. Med. **37**:21 (Jan. 1) 1937.

Wynkoop stresses the importance of breast feeding, especially in premature and delicate infants. A midafternoon lunch or milk at recess should be given only to malnourished children. It is difficult to keep a child's weight up without milk and cereals.

AIKMAN, Rochester, N. Y.

COMPARATIVE STUDY OF FAMILIAL AND INSTITUTIONAL PLACEMENT FOR CHILDREN. Rev. méd.-sociale de l'enf. **5**:47 (Jan.-Feb.) 1937.

The study concerns children who for reasons of health or because of scholastic difficulties need placement. Several possible types of placement are considered: in a family, in a small boarding home and in an institution. The various factors that must be considered in selecting children for placement, in choosing boarding homes and in evaluating the possible benefits offered by institutions are discussed. The possibility of securing a more fully rounded development (physical, scholastic and social) in a selected small boarding home is stressed.

DIETRICH, Los Angeles.

NUTRITION OF THE SCHOLARS IN A FEDERAL SCHOOL. R. DE SIQUEIRA, Arch. de pediat., Rio de Janeiro **9**:145 (Feb.) 1937.

The usual diet was given, which the author believes was adequate.

SANFORD, Chicago.

BIRTH RATE IN VIENNA. F. OLEGNIK, Wien. klin. Wchnschr. **50**:64 (Jan. 15) 1937.

Olegnik reports that the birth rate in Vienna has been decreasing since 1910. In that year the population was 2,031,498; in 1923, 1,865,780; in 1934, 1,860,308. The number of births per thousand inhabitants was: 1910-1911, 21.9; 1922-1923, 16.4; 1933-1934, 6.4. The excess of births over deaths changed from plus 4.5 per thousand inhabitants to plus 0.9, and finally to minus 6.1; i. e., at the present time there is an excess of deaths over births.

The birth rate varies in different months. If corrections are made for the variations in length of the different months, the following figures are obtained, each representing an average over several years: I, 104.5; II, 110.1; III, 110.1; IV, 109.4; V, 109.3; VI, 107.0; VII, 100.7; VIII, 90.7; IX, 94.4; X, 89.6; XI,

87.3; XII, 87.6. The number of births increases from February to May (with a peak in March). There is a smaller peak in September, with a considerable decrease toward the close of the year.

It is well known that the number of births varies at different times of day. Quetelet pointed this out in 1868. Raseri found that the comparative figures were 52 between 1 and 8 a. m. and 33 between 1 and 8 p. m. Stuart obtained the following figures: 12 midnight to 6 a. m., 29.1; 6 a. m. to 12 noon, 25.1; 12 noon to 6 p. m., 22.5; 6 p. m. to 12 midnight, 23.3. For Vienna, the results were: 11 p. m. to 5 a. m., 26.9; 5 to 11 a. m., 26.1; 11 a. m. to 5 p. m., 22.9; 5 to 11 p. m., 24.1.

Premature births were as follows: living males, 8.2 per cent; living females, 9.8 per cent; stillborn males, 53.4 per cent; stillborn females, 60.7 per cent.

To 100 births there were 2.9 stillbirths; of 100 babies who lived for two days, 2.6 died. Figures for the first year are as follows: first week, 0.7; second week, 2.5; third week, 1.6; fourth week, 1.9; second month, 5.1; third month, 4.7; fourth month, 3.8; fifth month, 3.9; sixth month, 2.8; seventh month, 2.4; eighth month, 2.0; ninth month, 1.5; tenth month, 1.5; eleventh month, 1.2; twelfth month, 1.0. Thus a large number of infants die during the first few weeks. Roesle ascribes the sharp increase of mortality during the second week to the fact that mother and child are dismissed from the hospital at this time.

ABT, Chicago.

## Prematurity and Congenital Deformities

ARACHNODACTYLY AND STATUS DYSRAPHICUS: A REVIEW. R. H. PINO, E. L. COOPER and S. VAN WIEN, Ann. Int. Med. **10**:1130 (Feb.) 1937.

Three cases of arachnodactyly are reported. Two of the reports concern boys aged 5 and 6 years, respectively. The third case was that of an adult. The purpose of the article is to confirm the views of Passow that arachnodactyly and status dysraphicus are very closely related, if not identical.

READING, Galveston, Texas.

A SECOND GROUP OF CASES OF ARACHNODACTYLY. R. LLOYD, Arch. Ophth. **17**:66 (Jan.) 1937.

In the *Archives of Ophthalmology* for May 1935 Lloyd reported six cases of arachnodactyly and now reports nine more. He has come to the conclusion that congenital bilateral dislocation of the lens is a part of the syndrome which when complete is one of typical arachnodactyly, although dislocation of the lens or skeletal changes may be missing.

WESCOTT, Chicago.

CHONDRODYSPLASIA. H. R. MAHORNER, J. Pediat. **10**:1 (Jan.) 1937.

Mahorner divides chondrodysplasia into four main groups: (1) Ollier's type, characterized by unilaterality; (2) hereditary deforming chondrodysplasia (Ehrenfried), characterized by many exostoses, broad metaphyses and frequently by a tendency to be hereditary; (3) Voorhoeves type, in which longitudinal striations of the metaphyses occur; (4) the Albers-Schönberg type, in which areas of increased density in the metaphyses and epiphyses are the most prominent feature.

In 9,442 admissions to the Hutchinson Memorial Clinic of Tulane University there have been 5 cases of chondrodysplasia (hereditary deforming type). These cases are reported and the clinical characteristics of this disease summarized. The first manifestations are generally noted in infancy. Males are more often affected than females. Along with hard irregular nodules on the skeleton, other deformities of the bone may occur. There are five characteristic roentgenologic features. The lesions are most marked in the metaphyses of the long bones in which most rapid growth is occurring. Abnormal findings are most marked in the rapidly growing bone, for in adult life healing tends to occur by uniformity

of ossification. Irregularity and incompleteness of ossification near the epiphyses are indicated by clear areas, streaking, striation and stippling of the metaphyses. The metaphyses are long, extending for an abnormal distance into the diaphyses with their smaller diameters. Exostoses may be prominent but in the x-ray picture their development is shown to be not the fundamental process.

Mahorner cites the various theories as to the etiology, and, except for the hereditary factor, none of them have been credited. He feels that the most reasonable explanation of the disease is that it represents a deficient anlage in the cells, suggesting a localized deficiency, such as a shortage of phosphatase, or some analogous explanation. Aside from surgical removal of the osteochondromas which become unsightly and interfere with function, there is no successful treatment of this disease.

RAUH, Cincinnati.

MATERNAL AND CHILD HEALTH WORK IN SOUTH CAROLINA. R. W. BALL, J. South Carolina M. A. **33**:6 (Jan.) 1937.

A composite review of the work done in South Carolina is given by Ball, who is the director of the maternal and child health divisions of the board of health of this state. He states the percentages of defects in babies with prenatal difficulties and in well babies. The statistics which he has compiled make it evident that there are far too many mortalities from childbirth and in infants. The data computed are a base from which work must begin in the hope that marked improvement will be shown in the next few years.

WESTON, Columbia, S. C.

PERSISTENT TRUNCUS ARTERIOSUS COMMUNIS WITH MICROPHTHALMOS, ORBITAL CYST AND POLYDACTYLY. H. A. HARRIS and G. C. THOMSON, Arch. Dis. Childhood **12**:59 (Feb.) 1937.

An infant girl of 6 days presented truncus communis arteriosus, complete failure of the pulmonoaortic septum, deficient ventricular and auricular septums, microphthalmos, orbital cysts and polydactyly. The site and nature of the anomalies point to an interference with normal growth during the fifth week of embryonic life, but the maternal history is without any relative incident.

KELLY, Milwaukee.

A NOTE ON LITHOPAEDION WITH REPORT OF A CASE. P. CAVE, Brit. M. J. **1**:383 (Feb. 20) 1937.

A brief description of lithopedion is furnished, with a classification embracing three types, followed by a report of a case. The woman was 83 years of age and had a pain in the left hip as the result of a fall. A roentgen examination to determine the type of fracture of her hip was made; shadows were found which were taken to be fetal bones. A few days later she died of cerebral hemorrhage. Autopsy was refused, but a postmortem roentgen examination of the body was permitted. This showed a lithopedion. From the history of the case it is thought that this lithopedion had been carried by the woman for fifty years.

ROYSTER, University, Va.

CHONDRODYSPLASIA. R. S. LEVINE, Rev. d'orthop. **24**:30 (Jan.) 1937.

Chondrodysplasia produces no antecedent symptoms, no pain, no atrophy, no paralysis. These are absent even when the condition is fully developed. The reflexes are normal. Girls are more frequently attacked than boys. Almost all of the bones of the body may be involved, though usually the clavicles and vertebrae remain free. The x-ray picture is essential in arriving at the diagnosis. The first apparent sign may be enlargement of the ends of one or more of the long bones, with slight lengthening. The x-ray picture shows enlargement of the lacunae of the diaphysis with thin bony trabeculae running between. In the case which Levine reports there was an associated ovarian tumor producing

early sex characteristics. The patient, a child of 4 years, showed the characters of sex of one approximately 14 years old. These disappeared after removal of a globulosarcoma of the ovary. The chondrodysplasia involved the tibia, femur and metatarsals on the right side, the right side of the pelvis more than the left, the scapulae, radii and ulnae, and the left metacarpals. The left side of the face was larger than the right, though the bones of the skull were apparently normal. On pathologic section, the bones showed long spindle-shaped cells, with a very cellular filament subcartilage. Treatment does not seem to alter the picture. The condition may regress spontaneously or may remain with slight progress.

RYAN, Vancouver, B. C.

HEREDITARY CRANIOFACIAL DYSOSTOSIS. C. CALDERIN, L. SCULL, R. MONTERO and A. GARCIA, Arch. de med. inf. **6**:89 (March) 1937.

This condition, also known as Crouzon's disease, was found in a Negro. As far as the authors are aware, the case is the first that has been described in that race. The child's father was dead, but relatives stated that he had the same cranial deformity. Photographs and roentgenograms of the child are shown. There is no treatment, but when blindness develops, the optic nerve should be freed from the anterior orifice of the optic canal, where it is choked.

SANFORD, Chicago.

CONSTITUTIONAL ANOMALIES. V. BAPTISTA, J. de pediat., Rio de Janeiro **4**:23 (Jan.) 1937.

Baptista discusses exudative diathesis and allergic diathesis.

SANFORD, Chicago.

COMPLETE SYNDACTYLISM OF THE HANDS AND FEET WITH OTHER DEFORMITIES. F. J. LICEAGA, J. de pediat., Rio de Janeiro **4**:51 (Feb.) 1937.

An 11 year old girl showed complete syndactylism of the hands and feet, cranial deformity, sinus arrhythmia with auricular-ventricular retardation, and intraventricular irregularities of conductivity. Photographs are shown to illustrate the condition.

SANFORD, Chicago.

PTERYGIUM COLLI IN THE FIELD OF MULTIPLE ANOMALIES. H. HOFFMANN, Arch. f. Kinderh. **110**:1, 1937.

Three cases of pterygium colli, a congenital abnormality in which folds of skin extend bilaterally from the mastoid process to the acromion, are reported, and cases recorded in the literature are reviewed. The condition is commonly accompanied by other congenital anomalies. Hoffmann believes that it is an abnormality of platysma myoides. Possible causes are discussed.

CRANE, Washington, D. C.

CONGENITAL PARTIAL GIGANTISM. H. HIPPE and K. HÄHLE, Röntgenpraxis **9**:116 (Feb.) 1937.

The patient whose case is reported was a 6 year old girl, the child of normal parents. The index finger and third finger of the left hand were prodigiously enlarged at birth and remained proportionately larger than their fellows up to the time of examination. From the age of 18 months onward progressive swelling occurred in the left upper arm. Roentgen examination revealed that the gigantic proportions of the fingers were due to hypertrophy of the bones of the phalanges; slight enlargement was noted in the left humerus. The bones of the right upper extremity were of normal caliber.

Cases of congenital partial gigantism have been reported by Frisch, Kaufmann, Windholz, Glanzer, Hilmi, Spreizer, Liebe and others. A distinction is made between true gigantism, in which the skeleton is also involved, and false gigantism, in which the soft tissues alone are affected. Appropriate references are supplied.

McCUNE, New York.

SYNDACTYLIA AND ITS TREATMENT. R. J. HARRENSTEIN, Maandschr. v. kindergeneesk. **6**:131 (Jan.) 1937.

Harrenstein discusses the different types of congenital malformation of hands and fingers and the endogenic and aminogenic causes of syndactylia. He mentions the greatly varying forms of syndactylia and stresses the simultaneous occurrence of syndactylia and other congenital malformations, such as contractions and stiffening of the finger joints. The different ways of operating for syndactylia are discussed, and the results in nine cases are reported and the report illustrated with photographs.

VAN CREVELD, Amsterdam, Netherlands.

## New-Born

PNEUMOTHORAX IN THE NEW-BORN. B. P. STORTS and H. C. JAMES, Arch. Pediat. **53**:744 (Nov.) 1936.

Pneumothorax involving the left side of the chest was observed in a 3 day old infant. An x-ray picture of the chest showed steep angulation of the left side of the diaphragm and the heart pushed over to the right side. Following administration of 5 per cent carbon dioxide in oxygen at frequent intervals for forty-eight hours improvement was noticed. An x-ray picture taken three weeks later showed the left lung completely expanded and the heart in its normal position. At the age of 8 weeks acute intussusception developed. Operation was performed, and the infant died thirty-six hours later. Permission for autopsy was not obtained.

ORR, Buffalo.

A FACE MASK FOR USE IN ADMINISTERING OXYGEN TO THE NEW-BORN. H. A. AGERTY and C. M. WITZBERGER, Arch. Pediat. **54**:101 (Feb.) 1937.

The authors described a face mask used for the administration of oxygen to the newly born.

ORR, Buffalo.

TETANY IN THE NEWBORN. C. E. SNELLING and A. BROWN, J. Pediat. **10**:167 (Feb.) 1937.

Seven cases of tetany in the new-born are described. The symptoms common to these cases were twitching, spells of cyanosis and convulsions. Cyanosis of the new-born is not infrequently a symptom of tetany.

Reviewing the cases of tetany seen in the Hospital for Sick Children, Toronto, in the years 1928 and 1935, the authors found the peak of the age incidence in the year 1928 to be in the period from 4 to 10 months, whereas in 1935 the incidence decreased from birth with advancing age. In 1928 thirty of the thirty-two cases occurred between January 1 and May 1. In 1935, though there was some increase between February and May, with the exception of August and September, there were one or two cases every month.

RAUH, Cincinnati.

EDEMA IN THE NEWBORN DUE TO PRELACTEAL FEEDING: REPORT OF FOUR CASES. G. N. KROST and I. M. EPSTEIN, J. Pediat. **10**:221 (Feb.) 1937.

Krost and Epstein report four cases of edema in the new-born following the use of a mixture of 5 per cent solution of dextrimaltose no. 1, which contains 2 per cent sodium chloride, and 5 per cent sodium citrate as a prelacteal feeding. In order to determine the edema-producing factor in this feeding, successive groups

of thirty new-born infants were placed on various combinations of the aforenamed mixture and other sugars, dextrimaltose no. 2 and beta lactose with and without sodium citrate and sodium chloride and dextrimaltose no. 1 alone. The results of these feedings showed that dextrimaltose is more hydrating than other sugars and that the use of dextrimaltose no. 1, which contains 2 per cent sodium chloride, with sodium citrate upsets the delicate balance of the water metabolism of the new-born infant, causing tremendous retention of water.

RAUH, Cincinnati.

HEMORRHAGIC DISEASE OF THE NEW-BORN. N. B. CAPON, Lancet **1**:431 (Feb. 20) 1937.

In the sixty-one cases reported there were five deaths. Thirty-six of the infants were girls and twenty-five were boys. In many cases pregnancy and labor were normal. In fifty-nine cases the average age of the child when bleeding began was 41½ hours; in the other two the onset was late, the children being 120 hours and 288 hours old, respectively.

The author's routine treatment is to give an intramuscular injection of blood (20 cc.). This is repeated in two hours if the child is restless or if hemorrhage recurs. Finally, if these measures are unavailing, transfusion is resorted to. No light is thrown on the etiology of the disease.

LANGMANN, New York.

SOME REMARKS ON ANTE-NATAL SUPERVISION. T. G. WILSON, M. J. Australia **1**:86 (Jan. 16) 1937.

Wilson was instrumental in inaugurating the prenatal clinic in the Adelaide Hospital, Australia, and recently made an analysis of the results. He finds that there is little, if any, effect on maternal mortality but does not feel that this should influence any one against the value of prenatal care. He finds that induction of labor and instrumental delivery have been markedly on the increase, and from his analysis of case records he concludes that they are frequently unwarranted. He therefore enters a plea for more conservatism in regard to induction of labor and a continuation and extension of prenatal care.

TENNEY, Madison, Wis.

RETINAL HAEMORRHAGE IN THE NEWBORN. F. RICHMAN, Proc. Roy. Soc. Med. **30**:277 (Jan.) 1937.

Richman carried out an ophthalmoscopic study of 513 new-born infants at the King's County Hospital, Brooklyn. The infants were from 1 to 8 days old.

She found amazing differences in the normal fundi of these new-born infants. The disks showed many variations. At least six groups could be distinguished, each having special characteristics, which she describes briefly. The color of the disk of a normal new-born baby is of a peculiar grayish tinge. There is a scientific reason for this, for which one must look into the embryology of the eye. There is complete absence of choroidal tessellation in the normal infant's eyeground. The fundus either is diffusely red, with no choroidal details showing, or is light colored, with a network of the vessels showing. Normally the foveal reflex is not seen.

Hemorrhages are of three main types: (1) bright red flame-shaped extravasations in the nerve fiber layer, which are most common and least damaging; (2) dull red, diffusely round hemorrhages lying in the deeper layers of the retina; (3) preretinal collections of blood, very dark red and well circumscribed, which last longest.

The author discusses the hemorrhages.

The incidence of hemorrhage in the entire group of 531 babies was 12.2 per cent. First born babies showed 17.5 per cent, as compared with 9.2 per cent in the subsequent babies.

In conclusion she is convinced that every infant is entitled to an examination of the eye at birth as a matter of routine.

WILLIAMSON, New Orleans.

GANGRENE OF THE FINGERS. G. BLECHMANN and KOHN, Nourrisson **25**:21 (Jan.) 1937.

Blechmann and Kohn report gangrene of the terminal phalanges of the thumb and middle finger of the left hand in a new-born infant. Spontaneous amputation occurred three weeks later. The possibility that this was syphilitic is mentioned. Antisyphilitic therapy was instituted despite negative results of serologic tests, on account of hepatosplenomegaly. The baby died at the age of 3½ months.

McCLELLAND, Cleveland.

ICTERUS OF THE NEW-BORN. G. L. HALLEZ, Nourrisson **25**:31 (Jan.) 1937.

Data are presented to show that jaundice of the new-born depends on two factors: (1) hemolysis of the excess number of red blood cells present at birth, causing a hemolytic type of icterus, and (2) hepatic insufficiency, which renders the organism unable to cope with the sudden cholemia brought about by tying off the cord and thus preventing excretion of bile by way of the placenta and the maternal circulation.

McCLELLAND, Cleveland.

SIALADENITIS OF THE PAROTID GLAND IN A NEW-BORN INFANT. DIAZ ORERO and B. SÁNCHEZ SANTIAGO, Arch. de med. inf. **6**:68 (March) 1937.

Suppurative inflammation of the left parotid gland was observed in an infant of 7 days. The authors believe that this was local rather than metastatic. The infant recovered rapidly after external incision.

SANFORD, Chicago.

MENSTRUATION IN A GIRL THREE DAYS OF AGE. M. C. CALERO, Rev. méd. latino-am. **22**:557 (Feb.) 1937.

The author reviews the theories concerning the funtional evolution of the uterine mucosa and the influence of the graafian follicle and corpus luteum on menstruation. Metrorrhagia is reported in a girl 3 days of age in whom there was no antecedent trauma or infection except that signs of hereditary syphilis were present and the Kahn test was positive. The blood chlorides and cholesterol were greatly increased. No conclusions are made as to the cause of the metrorrhagia.

DWYER, Kansas City, Mo.

THE POSITION OF THE OBSTETRICIAN CONCERNING THE QUESTION OF PERINATAL INFANT MORTALITY. E. WEINZIERL, Med. Klin. **33**:16 (Jan. 2) 1937.

Three aspects of the problem are discussed: (1) instruction of girls and women, (2) training of qualified obstetricians, midwives and nurses and (3) construction of institutions for prenatal, natal and puerperal care. The practice of obstetrics should be limited to obstetricians, because general practitioners are insufficiently trained and they are likely to transmit infections. Early prenatal care will reduce mortality from complications of pregnancy and will be beneficial from the standpoint of hygiene and nutrition. Regarding care of the infant, cooperation with the pediatrician is important.

SIEMSEN, Chicago.

INTRACRANIAL INJURIES OF INFANTS AT THE TIME OF BIRTH. H. KÜSTNER, Med. Klin. **33**:221 (Feb. 12) 1937.

To reduce the mortality among spontaneously born infants, which is due largely to prematurity, prenatal supervision and prevention of premature births are necessary. Intracranial injuries resulting from instrumental delivery can hardly be avoided without jeopardy to the mother. Good prenatal supervision and careful management of delivery are important.

In view of the physical and mental end-results, therapy of intracranial injuries cannot be encouraged.

SIEMSEN, Chicago.

CESAREAN SECTION WITH INTRACRANIAL HEMORRHAGE. T. BRANDER, Monatschr. f. Kinderh. **69**:68 (Feb.) 1937.

A 3,500 Gm. boy was delivered by cesarean section. He was deeply asphyxiated and cyanotic, and soon convulsions developed. Spasticity followed, and there was increased tension in the fontanel, although intraspinal pressure was not increased nor could blood be found in the spinal fluid. Death occurred on the fourth day, and autopsy showed extensive cerebral hemorrhage. GERSTLEY, Chicago.

VITAMIN C CONTENT OF THE URINE AND FECES OF NEWLY BORN INFANTS. T. ISHIBASHI, Acta pædiat. japon. **43**:187 (Feb.) 1937.

Ishibashi estimated the vitamin C in the urine and feces of new-born infants, using Fujita's colorimetric method. The results obtained led to conclusions as follows: 1. The vitamin C of the urine decreases as the infant grows older. 2. Although the amount of vitamin C in acid urine is greater than that in alkaline urine, the vitamin in acid urine is not necessarily high. 3. The vitamin C of the feces increases as the infant grows. 4. There is no relation of the amount of vitamin C in the stools to their color, although no vitamin C was demonstrable in meconium. 5. In each infant there is no constant change in the amount of vitamin C in the feces, while the urine shows a gradual decrease. 6. Injection of vitamin C causes an increase of vitamin C in the urine, demonstrable in thirty minutes, reaching the highest peak in from two to four hours and returning to normal values in from seventeen to twenty-one hours; no such constant relations were seen in feces. 7. In severely sick infants injection of vitamin C produces no rise in vitamin C in the excreta and in moderately sick children the rise in vitamin C in the excreta is decidedly less than that in normal infants.

KATO, Chicago.

CONGENITAL MALARIA. C. J. W. BISDOM, Maandschr. v. kindergeneesk. **6**:199 (Feb.) 1937.

Congenital malaria was found in an infant of 25 days. The mother suffered from the disease during pregnancy. Fever was absent in the infant, and there was a tendency to hypothermia. Severe anemia and an important enlargement of the spleen developed. According to recent conceptions, malaria parasites are able to pass through the placenta. VAN CREVELD, Amsterdam, Netherlands.

HYPOGLYCEMIA OF THE NEW-BORN AND THE COURSE OF DIABETES IN THE MOTHER. A. ALKEMA, Nederl. tijdschr. v. geneesk. **81**:681 (Feb. 13) 1937.

Alkema describes hypoglycemia of a new-born infant of a diabetic mother. The infant had been treated successfully with dextrose. He also describes the course of the diabetes of the mother.

VAN CREVELD, Amsterdam, Netherlands.

## Acute Contagious Diseases

ECZEMA VACCINATUM. JAMES WILLIAM TEDDER, Arch. Dermat. & Syph. **34**:1008 (Dec.) 1936.

The occurrence of generalized vaccinia is extremely rare in relation to the frequency with which vaccination is performed. The clinical features of Kaposi's varicelliform eruption, pustulosis vacciniformis (varioliformis) acuta, and eczema vaccinatum are identical. Eczema, by lowering the immunity of the skin, affords good soil for the growth of the virus. There seems to be an upset in the balance between the virus and the virucidal substances, which causes more organisms to enter the circulation of eczematous patients. The final outcome which, because of the seriousness of the disease, requires a guarded prognosis, depends on the ability

of the antivirus substances to cope with the increased amount of virus. Eczema vaccinatum in most instances represents exogenous inoculation, even though such a history is difficult to obtain.

DULIN, Iowa City.

ACUTE THROMBOCYTOPENIC PURPURA FOLLOWING VARICELLA. HARRY J. COHEN, Arch. Pediat. **53**:773 (Dec.) 1936.

The author reports a case of thrombocytopenic purpura of the symptomatic type following chickenpox in a boy aged 6½ years. The patient made a complete recovery, and there has been no return of symptoms.

ORR, Buffalo.

COMPLEMENT FIXATION TESTS IN PERTUSSIS. M. WEICHSEL and H. S. DOUGLAS, J. Clin. Investigation **16**:15 (Jan.) 1937.

The complement fixation test described in this paper gave positive results in about 80 per cent of the cases of whooping cough in children over 1 year of age and after the second week of cough. The test remained positive for about five to eight months. In about 90 per cent of normal children it was negative irrespective of a previous history of pertussis; 5 per cent gave doubtful and 5 per cent gave positive results. In at least 13 per cent of normal healthy adults positive reactions were observed.

GUEST, Cincinnati.

VITAMIN C THERAPY AND PROPHYLAXIS IN EXPERIMENTAL POLIOMYELITIS. C. W. JUNGEBLUT, J. Exper. Med. **65**:127 (Jan.) 1937.

For a number of years Jungeblut has contended that success in the control of infantile paralysis must depend on the accumulation of more precise knowledge regarding the mechanism of natural protection against this disease. Once it is clearly understood why the majority of children and an even greater proportion of adults fail to contract paralysis on exposure to the infectious agent, or why certain exceptional children are so highly susceptible that their first contact with the virus leads to invasion of the central nervous system, it may be possible to apply the same principles to the therapy and prophylaxis of the disease.

He discusses the two opposing theories that have been invoked to explain the mechanism of this natural resistance. The immunization theory regards all persons as primarily susceptible and attributes protection exclusively to acquired specific immunity. The so-called maturation theory, on the other hand, holds that man under natural conditions of infection is normally insusceptible and can carry the virus with impunity and that production of the disease, which occurs only in comparatively few persons in spite of widespread chances for infection, is brought about by some transient physiologic abnormality or deficiency, hormonal or nutritional in character.

Jungeblut believes that the known facts agree better with the theory of physiologic resistance than with the assumption of an almost universal latent immunization.

A summary of the results shows (*a*) that among sixty-two treated monkeys nineteen survived without paralysis and forty-three succumbed to the disease, while among thirty-eight untreated controls only two failed to show paralysis and thirty-six succumbed to the disease, and (*b*) that treatment with large doses of vitamin C was without any beneficial effect (all ten monkeys which had received from 700 to 100 mg. presenting paralysis), that the administration of intermediate doses was followed by occasional survival without paralysis of the treated animal (three of nineteen monkeys which had received from 50 to 10 mg. surviving), and that nearly one half of the animals which had received small doses escaped the disease (sixteen of thirty-three monkeys which had received 5 mg. surviving).

Attempts to protect monkeys against subsequent intracerebral infection by prophylactic administration of vitamin C either per os or parenterally have produced negative results.

KNICKERBOCKER, Dallas, Texas.

EFFECT OF THE CHEMICAL CONSTITUTION OF SOAPS UPON THEIR ACTION ON DIPHTHERIA TOXIN. M. BAYLIS, J. Infect. Dis. **59**:131 (Sept.-Oct.)) 1936.

Baylis found that diphtheria toxin is neutralized by nearly all soaps. The degree of effectiveness varies with the chemical constitution. Sodium chaulmoograte and sodium ricinoleate are the most efficient neutralizers. Bile salts, although recognized for a long time as good toxin neutralizers, were very inefficient.

TOOMEY, Cleveland.

RELATIONSHIP BETWEEN NASAL AND HUMORAL ANTIPOLIOMYELITIC SUBSTANCES. B. F. HOWITT, J. Infect. Dis. **60**:113 (Jan.-Feb.) 1937.

In vitro neutralization tests were positive on thirty-six (59 per cent) of the serums and fourteen (22.9 per cent) of the filtered nasal washings from sixty-one persons. No particular correlation could be made between a positive result with serum and a positive result with the nasal filtrate, although more of the nasal filtrates giving positive results were obtained among so-called normal adults than among persons recovered from poliomyelitis. Nine persons had positive results in both serum and nasal filtrates; five showed antiviral washings with serums that gave negative results, while twenty-seven had positive results in the serum and negative results in the filtrates.

About as great a number of filtrates giving positive results were found among those with abnormal nasal conditions as among those with normal.

Seventy-one and three tenths per cent of the normal adults had antiviral serum as compared with 60 per cent of those recovered from poliomyelitis, while 55 per cent of normal children had antiviral serum as compared with 40 per cent of the recovered poliomyelitic group.

Concentration of nasal filtrates by the Flosdorf and Mudd lyophil apparatus was of value in securing more positive neutralization tests.

No antiviral substances were found in the nasal washings of five immunized monkeys taken at different stages of immunity. Their tissue immunity failed to run parallel with the humoral response, since three animals had neutralizing antibodies in the serum without resistance to intracerebral inoculation of virus.

TOOMEY, Cleveland.

PLACENTAL EXTRACT (IMMUNE GLOBULIN—HUMAN) WITH SPECIAL REFERENCE TO ITS USE IN THE PREVENTION AND MODIFICATION OF MEASLES. R. C. ELEY, J. Michigan M. Soc. **35**:769 (Dec.) 1936.

An address presented at the seventy-first annual meeting of the Michigan State Medical Society.

CAREY, Detroit.

TREATMENT OF INFANTILE PARALYSIS. A. D. LAFERTÉ, J. Michigan M. Soc. **35**:782 (Dec.) 1936.

LaFerté discusses the management of the second stage, or convalescence phase, of the disease.

CAREY, Detroit.

PLACENTAL FLUID IN MEASLES PROPHYLAXIS. S. KARELITZ, C. K. GREENWALD and A. J. KLEIN, J. Pediat. **10**:170 (Feb.) 1937.

The authors found that the diphtheria antitoxin titer of the fluid expressed from the human placenta together with the blood expelled with the placenta is identical in most instances with that of the corresponding maternal blood serum. This suggested the possibility that measles antibodies are also distributed in the same measure in placental fluid and in maternal serum. Placental serum was used in prophylaxis against measles in doses equal to those of immune adult blood. The results were compared with the results expected had the immune adult blood been used. The placental fluid was obtained from women who definitely had had measles.

The placentas, collected with the expelled blood, were cut into small pieces and squeezed in a simple fruit press. The fluid was centrifugated and the supernatant fluid treated with merthiolate. Some of the salts were removed by dialysis. Hematin and acid proteins were removed by acidification. In one sample these proteins and hematin were not removed, in order to discover whether any reaction was caused by the injection of these substances. Following the precipitation of the hematin and acid proteins the fluid was brought to a $p_H$ of 6.8 by the addition of normal sodium hydroxide, filtered and tested for sterility before use. Sixty-four children exposed to measles in the home were treated, and the placental fluid was found to be effective in prophylaxis against measles in doses equal to those of immune adult serum. Two thirds of the treated children had mild or moderate reactions such as local pain and local heat and redness at the sites of injection. In a few cases general reactions, such as nausea and fever up to 101 F., occurred. One child had an attack of asthma, and two children showed local urticaria. No striking difference in reaction was noted in the use of the fluid from which the hematin and acid proteins had been removed. Aging of the fluid from five to six months resulted in less reaction without any demonstrable loss in prophylactic value.

RAUH, Cincinnati.

MULTIPLE NEURITIS FROM DIPHTHERIA TOXOID: REPORT OF A CASE. S. J. WILKINSON, J. Pediat. **10**:180 (Feb.) 1937.

Alum-precipitated toxoid, 0.5 cc. of a proprietary commercial brand, was given to a year old girl. At the time of the injection she was thought to have a slight cold in the head, though examination revealed no evidence of infection. Two and a half weeks prior to the inoculation she suffered from a mild attack of measles, which was modified by the use of parental blood. During the three weeks following the injection of toxoid, she gradually began to show paresis and hypotonicity of the voluntary muscles with absence of the deep and abdominal reflexes. No mental changes were noted, and the extra-ocular movements, pupillary reflexes and gag reflexes remained normal. Speech and swallowing were unaffected. Three weeks after the inoculation the nodule at the site of injection of the toxoid was removed. Improvement in the child's condition began one month after onset and continued slowly until complete recovery occurred.

The author discusses the differential diagnosis and believes that the peripheral nerve paralysis in this case belongs to that group of paralyses which follow the use of therapeutic and prophylactic serums and vaccines, such as typhoid and staphylococcus vaccine, diphtheria, tetanus and pneumonia antiserums and immunizing toxins such as that of scarlet fever. This is the first case of multiple neuritis following the use of diphtheria toxoid to be reported.

RAUH, Cincinnati.

SEVERE VISCERAL COMPLICATIONS IN ANTERIOR POLIOMYELITIS: CASE REPORT. B. L. KEYES, J. Pediat. **10**:233 (Feb.) 1937.

A 13 year old boy with acute anterior poliomyelitis showed almost complete paralysis of the muscles of all four extremities, neck, chest and abdomen and paralysis of the intestines, rectum and bladder. The urine early in the disease contained albumin, pus cells, granular cells and casts. Hematuria was noted on numerous occasions. The specific gravity of the urine varied between 1.010 and 1.003. The blood chemistry was not abnormal. The blood pressure was elevated to from 150 to 130 systolic and 110 diastolic.

There was gradual improvement in the muscle paralysis but no improvement in the urinary symptoms. The hematuria persisted, the blood pressure remained elevated, nausea occurred, and following a series of generalized convulsions the patient died.

Autopsy revealed hydronephrosis, acute ascending pyelonephritis, hemorrhages in the collecting tubules, and pink staining and granular precipitation in the capsular spaces and in the tubules.

RAUH, Cincinnati.

ATYPICAL POLIOMYELITIS WITH UPPER NEURONE INVOLVEMENT. SAMUEL L. IMMERMAN, M. Rec. **144**:511 (Dec. 2) 1936.

A case of atypical poliomyelitis with involvement of the upper neurons is reported in a girl of 14. The case is of interest because atypical symptoms, chiefly change of personality and rigidity, led to a diagnosis of hysteria.

On the day when the patient commenced to complain, she had had a slight accident in turning a somersault, and her first symptoms—stiffness of the entire back, the neck and the knees and headache—were thought to be due to this.

A full report of the case is given in the paper.

WILLIAMSON, New Orleans.

PROPAGATION OF VARIOLA VIRUS IN THE DEVELOPING EGG. A. S. LAZARUS, B. EDDIE and K. F. MEYER, Proc. Soc. Exper. Biol. & Med. **36**:7 (Feb.) 1937.

Vesicular fluid from lesions in a typical case of smallpox was injected into the chorio-allantoic membrane of the developing egg, and the propagation of the virus has been carried through forty-five consecutive passages. Discrete yellowish white lesions were observed on the membrane. Smears treated with Morosow's stain showed typical Paschen bodies. No bacterial contaminations were encountered, and no dead embryos were observed. No lesions of the skin of an embryo have been noted, although some necrotic areas have been seen in the liver in heavily infected eggs. Fragments of the membrane, dried, were found by Craigie to give complete fixation with an S serum but only partial fixation with an L serum, probably owing to deterioration of the L antigen as a result of incomplete drying. The presence of the virus was further confirmed by staining preparations with victoria blue by the method of Herzberg.

HANSEN, Minneapolis.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **51**:1733 (Dec. 18) 1936.

For the period from November 1 to 28 the incidence of poliomyelitis showed a marked decline, although it was still in excess of that for the same period in any of the last three years. Smallpox, influenza, typhoid, scarlet fever, measles and diphtheria all continued to occur infrequently. The number of cases of meningococcic meningitis rose to 378, which is the highest incidence since 1929. The average rate of deaths from all causes in large cities was 11.5 per thousand.

SANFORD, Chicago.

HISTORY AND FREQUENCY OF DIPHTHERIA IMMUNIZATIONS AND CASES IN 9,000 FAMILIES. SELWYN D. COLLINS, Pub. Health Rep. **51**:1736 (Dec. 18) 1936.

The information making up this report was obtained between 1928 and 1931 in eighteen states.

Among children less than 15 years of age, there was immunization in 30.5 per thousand. Immunization was as frequent in rural areas as in urban, but attacks of diphtheria occurred more frequently in large cities. In children of preschool age the frequency of immunization increased with the income of the family. The peak of mortality from diphtheria occurred among 2 year old children.

There are many tables and graphs in the report that should prove of value to any one interested in the subject.

SANFORD, Chicago.

A REVIEW OF RECENT WORK ON WHOOPING COUGH. R. E. SMITH, Quart. J. Med. **5**:307 (July) 1936.

A discussion of recent contributions on the subject of whooping cough is well presented by Smith. The subject is discussed under the following headings: (a) incubation period and mode of infection, (b) length of infectivity, (c) treatment and (d) summary.

Clinical protocols of twenty-six cases are also given.

BRADFORD, Rochester, N. Y.

BIOLOGICAL RELATIONSHIP BETWEEN ERYSIPELAS AND SCARLET FEVER. M. J. FOX. Wisconsin M. J. **35**:797 (Oct.) 1936.

Although there are marked differences, both clinically and in the immunity produced, between scarlet fever and erysipelas, Fox believes that there is a close etiologic relationship between the two diseases. He presents protocols of eleven cases, carefully controlled, in which persons exposed to scarlet fever presented erysipelas, or in which the reverse occurred.

Literature is cited supporting the contention that the various strains of Streptococcus haemolyticus causative of these conditions may under suitable circumstances undergo mutation to the extent of producing a different disease entity.

In an experience with 5,742 cases of scarlet fever Fox did not see a single instance of erysipelas occurring after convalescence in a patient who had been afflicted with scarlet fever. Furthermore, those patients with erysipelas who were treated with pooled human convalescent serum showed prompt improvement.

JANNEY, Wauwatosa, Wis.

ERYTHROCYTE SEDIMENTATION RATE IN SCARLET FEVER AND ITS COMPLICATIONS. J. S. COOKSON, Brit. J. Child. Dis. **33**:251 (Oct.-Dec.) 1936.

This is a record of the performance of the erythrocyte sedimentation test at various stages of scarlet fever in seventy-six cases. Antitoxic serum was given to the more severely ill patients on admission.

Büchler was the first to report on the erythrocyte sedimentation rate in scarlet fever. He described a curve gradually declining from an initially elevated level to reach normal figures on about the twenty-fifth day of the disease.

In this series normal figures were found in only a small number of cases as early as the twenty-fourth day of disease. Also in most cases in which complications developed the figures reached at the time of the complications were far in excess of the readings at the beginning of the disease.

A modified Westergren method was used, and 2 mm. in one hour and 5 mm. in two hours for men and up to 10 mm. for women were regarded as average.

There were thirty-five cases in which the disease was uncomplicated and thirty-seven in which it was complicated.

In the cases in which the disease was uncomplicated the rate was determined on the fourth, fourteenth and twenty-fourth days. A considerably raised rate on the fourteenth day of the disease means either that complications have already developed or will do so.

The complications included benign albuminuria (fourteen cases) nephritis (seven cases), otitis media (ten cases) and cervical adenitis (eight cases).

Of twenty cases in which the disease was uncomplicated and treatment was with serum a serum rash developed in six, but in these there was no corresponding rise of the curve such as one would expect with an allergic reaction of this nature.

The erythrocyte sedimentation rate was useful in differentiating types of albuminuria. A high rate meant that the patient had nephritis. The rate was a useful index of the efficacy of treatment.

LANGMANN, New York.

STREPTOCOCCAL PERITONITIS COMPLICATING SCARLET FEVER. D. ERSKINE, Brit. J. Child. Dis. **33**:272 (Oct.-Dec.) 1936.

An 18 month old boy on the second day of scarlet fever received 10 cc. of antiscarlatinal serum. On the twentieth day of illness he began to have occasional cyanotic attacks; then, vomiting and abdominal distention. A diagnosis of peritonitis was made and laparotomy performed. A large amount of clear peritoneal fluid was found, which gave a pure growth of the hemolytic streptococcus on culture. The child died ten hours after operation.

At autopsy a fairly large mass of chronic inflammatory tissue was found in the ileocecal angle. In this there were several enlarged mesenteric glands, one of which had suppurated. There was no evidence of appendicitis.

A review of the literature indicates that peritonitis complicating scarlet fever is rare but that inflammation of the mesenteric glands is more common than has hitherto been realized.

LANGMANN, New York.

CANCRUM ORIS FOLLOWING MEASLES. L. H. MACFARLANE, Brit. J. Child. Dis. **33**:275 (Oct.-Dec.) 1936.

A 3 year old boy had a mild attack of measles, and two days after the disappearance of the rash a swelling of the lower lip developed. A small necrotic area inside the lower lip was noticed. The necrosis spread rapidly, and the temperature was persistently high. The swelling spread to the whole cheek, left side of the neck and upper wall of the left side of the chest. Death occurred six days after the start of the gangrenous process. Smears from the necrotic areas inside the mouth, taken and examined after death, showed gram-positive and gram-negative organisms but no spirilla. A blood smear showed 78 per cent polymorphonuclear cells.

LANGMANN, New York.

INFECTION OF THE AIR OF SCARLET FEVER WARDS WITH STREPTOCOCCUS PYOGENES. W. A. BROWN and V. D. ALLISON, J. Hyg. **37**:1 (Jan.) 1937.

The air of four large scarlet fever wards was found to contain large numbers of hemolytic streptococci, most of which could be identified serologically. In general, types 1, 2 and 4 (85 per cent Streptococcus pyogenes) predominated, which corresponds to the finding in regard to types causing scarlet fever in London. There was partial correlation with the types infecting patients in the wards in which blood agar plating was done. Streptococcus pyogenes constituted about 10 per cent of the total bacterial growth. The degree of infection of the air showed much variation during the twenty-four hour period. At night it was negligible, with a steep rise in the morning, when ward activity was greatest, and with a moderate drop in the more quiet afternoons.

While transmission by infected hands, books, toys and other objects and droplet transmission may be more important, the authors feel that the air as a source of infection, especially in a ward, cannot be dismissed.

JANNEY, Wauwatosa, Wis.

THE ENDOTOXIN OF THE MENINGOCOCCUS. G. F. PETRIE, J. Hyg. **37**:42 (Jan.) 1937.

By experiments on the guinea-pig, rabbit and horse the authors have demonstrated that the endotoxin of the meningococcus is an intracellular poison and that it is one of a group of thermostable poisons present in various bacterial species. Repeated doses of the endotoxin failed to confer immunity to the pathogenic action of the toxin. Nor did the serums from the treated animals confer immunity against the endotoxin when serum-toxin mixtures were injected intracerebrally or intracutaneously into the guinea-pig. In contrast, experiments with three neurotoxins (diphtheria toxin, tetanus toxin and scorpion venom) in which specific serum-toxin mixtures were injected directly into the brains of guinea-pigs showed that lethal doses of these poisons could be neutralized. The conclusion drawn was that meningococcic endotoxin is not antigenic. The term "endotoxin" is not considered apt, since the poison seems incapable of causing the appearance of antigenic substances. The meningococcic endotoxin is both heat stable and resistant to chemical treatment. It is not changed by a temperature of 100 C. for half an hour or by action of a 0.5 per cent dilution of solution of formaldehyde at 37 C. for one month; nor can it be oxidized easily or disturbed by enzymic action. The endotoxin does not pass through a cellophane membrane.

The value of antimeningococcus serum in the treatment of cerebrospinal fever in man is apparently due to its antibacterial mechanism.

JANNEY, Wauwatosa, Wis.

INTRADERMAL TESTS FOR SUSCEPTIBILITY TO WHOOPING COUGH. B. O'BRIEN, Lancet **1**:131 (Jan. 16) 1937.

A series of 371 babies were examined for susceptibility to whooping cough by an intradermal test in which Sauer's vaccine is used as an antigen. The results showed a high measure of correlation in patients having nonimmune reactions, 90 per cent of whom had no previous history of whooping cough.

Certain incidents — the insusceptibility of positively reacting, i. e., immune, patients after exposure to infection, and the change of the reaction from negative to positive after an attack of whooping cough—support the view that the test is within limits a reliable index of susceptibility to infection with Haemophilus pertussis.

LANGMANN, New York.

THE DIAGNOSIS OF WHOOPING COUGH. J. P. PATON, Lancet **1**:132 (Jan. 16) 1937.

The complement fixation test is of value in confirming the clinical diagnosis of whooping cough. In atypical cases the test may by itself establish the diagnosis of pertussis by conversion of a negative to a positive reaction during the course of the illness. The complement fixation test becomes positive early in the infection in a high proportion of cases.

Negative results were most commonly obtained in very young children, in whom there seems to be a poor antibody response. Other apparent causes of negative reactions were short duration of the disease, very severe infection or presence of complications, and anticomplementary serum.

The intradermal test failed to give specific results. A high percentage of patients with whooping cough gave positive reactions, but so also did a group of control patients with no history of whooping cough.

LANGMANN, New York.

THE NEUTRALIZING VALUE OF POLIOMYELITIS CONVALESCENT SERUM FROM 1934 EPIDEMIC IN DENMARK. G. HARDY EAGLES, C. JENSEN and E. J. HENNINGSEN, Lancet **1**:462 (Feb. 20) 1937.

The protective value of human convalescent serum collected at the time of the Danish epidemic in 1934 was investigated by means of neutralization tests in monkeys. Separate pools had been obtained from patients with abortive poliomyelitis, nonparalytic patients and paralytic victims from thirteen to twenty-nine days after the onset of the meningitic state and compared with similar pools collected about four months later. Some evidence was obtained that pooled serum taken very early from nonparalytic patients and those with abortive attacks may have higher neutralizing value than that from paralytic patients, but this was not sufficiently definite to be convincing. Serum taken early in convalescence (at from thirteen to twenty-nine days) did not seem to have any greater neutralizing value than that taken later (four months). Pooled normal serum and serum from convalescents of long standing also contained viricidal antibodies in amounts not significantly less than serum taken early in convalescence.

LANGMANN, New York.

LOCAL BOARD OF HEALTH HINDMARSH: REPORT ON DIPHTHERIA IMMUNIZATION CAMPAIGN. J. M. DWYER, M. J. Australia **1**:273 (Feb. 20) 1937.

This is a summary of methods employed by the health department of Hindmarsh in organizing and carrying out a quick campaign of immunization against diphtheria. It was found that with a well organized team one physician could do 120 inoculations an hour. They used the unmodified toxoid because of the feeling that the results with repeated inoculations were better than those with the one injection of alum-precipitated toxoid. Reactions were very few, and the reduction in the incidence of diphtheria among the immunized was very satisfactory in the short time that had elapsed since the program was started.

TENNEY, Madison, Wis.

THE USE OF ARSENICALS IN DIPHTHERIA CARRIERS. A. IANCOU, TURCOU, DARIOU and DAVID, Nourrisson **24**:359 (Nov.) 1936.

Successful treatment of diphtheria carriers in child welfare institutions by nasal instillation of aqueous solutions or suspensions of several arsenical preparations is reported. Neoarsphenamine was found to be one of the most potent of those used. Merely nasal instillations were found effective in both infants and adults, but in some cases the lesions were considerably more rebellious to treatment.

McCLELLAND, Cleveland.

SEVERE LARYNGITIS OCCURRING LATE IN MEASLES. R. DUPÉRIÉ, Progrès méd., Dec. 12, 1936, p. 1947.

The incidence of laryngitis late in measles varies with the epidemic. It usually develops on the third or fourth day after the eruption and is not to be confused with the earlier catarrhal stage. The virus of measles renders the mucous membranes of the larynx susceptible to secondary invaders. It was thought at one time that the organism producing this ulcerative and membranous condition of the larynx in measles was the diphtheria bacillus, but many other organisms cause a similar picture. Intubation or tracheotomy may be necessary. The prognosis is bad, and if recovery takes place there are frequently scarring and stenosis of the larynx.

LESLIE, Evanston, Ill.

ELECTROCARDIOGRAPHIC STUDIES OF CARDIAC FUNCTION IN SINUS ARRHYTHMIA OF DIPHTHERIA. V. MENGOLI, Arch. ital. di pediat. **4**:612 (Dec.) 1936.

Mengoli studied thirty-eight children who showed sinus arrhythmia during convalescence from diphtheria. The ages ranged from 2 months to 12 years. Electrocardiograms were made before and after exercise during convalescence and again several months after cure. Exercise caused the arrhythmia to disappear in 52.7 per cent of the cases; but in ten of the remainder it caused accentuation. Neither the disappearance nor the accentuation seemed to indicate the condition of the myocardium. Diphtheria did not accentuate the arrhythmia which was present before the illness. Exercise evoked extrasystoles in two children and auricular-ventricular dissociation in a third. It did not influence the form of the P wave, the QRS complex or the PR relationship. Alterations in the T wave appeared to be of significance only in cases of abasement. Sinus arrhythmia was associated with electrocardiographic changes in 23.6 per cent, and all of the changes regressed with cure.

DOOLEY, New York.

POSTVACCINAL ENCEPHALITIS IN INFANTS. G. RIGGIO, Lattante **7**:614 (Dec.) 1936.

Riggio reports a case of encephalitis in a 9 month old boy. On the third day after vaccination, the vesicle began to form; on the fourth day, the symptoms of encephalitis appeared; very high temperature, vomiting and convulsive movements of the face and of the right arm and leg persisted for five days. The spinal fluid showed 26 cells, a positive reaction in the Pandy test and a normal amount of sugar. The treatment was by nonspecific protein therapy—injections of milk. Three months later, the only residual sign was slight limitation of motion of the right hand.

HIGGINS, Boston.

EXPERIMENTAL RESEARCHES ON THE RECIPROCAL ACTION OF DIPHTHERIA BACILLI AND HUMAN LEUKOCYTES IN THE PRESENCE OR ABSENCE OF ANTITOXIN. P. RITOSSA, Pediatria **45**:1 (Jan.) 1937.

Ritossa describes vividly the reciprocal action of human leukocytes on diphtheria bacilli in vitro and the lytic action of the latter on the leukocytes. He illustrates his article with photomicrography showing the different phases of the process. He has noticed in a mixture of diphtheria bacilli and leukocytes a

diminution in the number of leukocytes due to a leukocytolytic action of the diphtheria bacilli and, on the other hand, the intense phagocytosis of the diphtheria bacilli by the leukocytes. In this biologic struggle many of the phagocytes degenerate and die. On adding diphtheria antitoxin to the mixture of diphtheria bacilli and leukocytes, the leukocytosis is attenuated, the phagocytes are made more resistant and the action of defense more vigorous.

PALMIERI, Brooklyn.

ENCEPHALOMYELITIS DURING AND FOLLOWING MEASLES. A. GRASSI, Riv. di clin. pediat. **34**:1069 (Dec.) 1936.

Grassi reports three cases of encephalitis and one of encephalomyelitis following measles and one case of encephalitis occurring during the course of measles. Of the cases of encephalitis which followed measles, one was characterized by headache, asthenia and transitory paralysis; the second, by convulsions with some residual involvement; the third, by inability to walk well and increased intracranial pressure, and the fourth, by choreiform movements. In each of these there was practically complete recovery. In the case in which the disease occurred during measles, Koplik's spots were visible, but no exanthem appeared. The child had convulsive movements, which were followed by coma and death.

The author believes that in the first four cases an encephalitic virus was present in the system and became active as a result of infection with measles.

HIGGINS, Boston.

PROBLEMS IN POLIOMYELITIS—MENINGEAL FORMS OF HEINE-MEDIN DISEASE. R. CIBILS AGUIRRE, Bol. Inst. internac. am. de protec. a la infancia **10**:331 (Jan.) 1937.

The author underlines the capital importance of a differential diagnosis, in order to formulate an early diagnosis, with prognosis and treatment of the meningeal forms of Heine-Medin disease.

That there are meningeal forms is a fact, and the diagnosis of these forms may be established by clinical observation, humoral and pathologic-anatomic investigations and animal experimentation. Their knowledge does not have a purely doctrinarian or speculative purport but chiefly a practical one. It enables them to discover the nonparalytic forms of the poliomyelitic infection. The meningeal forms mark the beginning of the preparalytic period, and to know this is to win all the advantages of an early diagnosis. Of course, if one waits for the classic paralysis to appear in order to make a diagnosis, the latter will come by itself, but it will unfortunately come late, when the drama is almost finished.

FROM THE AUTHOR'S SUMMARY.

ANTIPERTUSSIS SERUM. JOSE M. DA ROCHA and JOSE A. B. NOGUEIRA DA GAMA, J. de pediat., Rio de Janeiro **3**:558 (Dec.) 1936.

The authors used a bovine antipertussis serum prepared by Genesio Pacheco of the Oswaldo Cruz Institute in the treatment of five carefully observed cases of pertussis. Injections of from 3 to 5 cc. were given at intervals of three days. The results were considered favorable.

SANFORD, Chicago.

ACTION OF THE HORMONE OF THE ADRENAL CORTEX ON DIPHTHERITIC INTOXICATION. G. MELODIA, Med. inf. **7**:357 (Dec.) 1936.

A preparation of adrenal cortex, made according to the directions of Swingle and Pfaiffer, was used in these studies. When injections of this and a minimum lethal dose of diphtheria toxin were simultaneously given to guinea-pigs, no protection was found, and the animals died after the same period of time as when no cortical substance was given. Giving adrenal cortex before, or at frequent intervals after, the injection of the toxin also gave no protection.

When cortical extracts and diphtheria toxin were mixed and kept at a temperature of 37 C. for one hour before injection, the animals did not die. This neutralizing of the toxin was probably due to the lipoids in the cortical extract.

HIGGINS, Boston.

PREVENTION AND ATTENUATION OF MEASLES BY THE USE OF HUMAN PLACENTAL EXTRACTS. R. L. CID and A. PULIDO, Rev. chilena de pediat. **8**:91 (Feb.) 1937.

A series of 112 susceptible children who had been exposed to measles were treated with extracts of human placental globulins. The dose injected intravenously was from 6 to 10 cc., depending on the time which had elapsed since exposure. In 72 per cent of the subjects the disease was prevented. Eleven per cent had only an attenuated attack. When the injection was given within the first one or two days after exposure, there were no failures, and only 4 per cent when it was given within four days. In contrast to the effects which follow the injection of whole placental extract, no reactions, either local or general, were observed. The authors recommend injection of larger doses than those advocated by some American authorities.

SCHLUTZ, Chicago.

RESULTS OBTAINED WITH COWPOX SERUM IN THE TREATMENT OF WHOOPING COUGH. R. AGRELO, Rev. méd. latino-am. **22**:521 (Feb.) 1937.

Agrelo reviews briefly the literature on the effect of various infections on whooping cough and especially the influence of vaccination against smallpox. In this study the serum of calves vaccinated against cowpox was used. Fifty children with whooping cough, divided into three groups according to the duration of the disease, received one or two injections of the serum in 5 or 10 cc. doses. All responded to this procedure; those with whooping cough in an early stage responded within fifteen days. In the controls whose disease was without complications the duration was from sixty-three to eighty-four days.

DWYER, Kansas City, Mo.

ENCEPHALITIS WITH MEASLES. H. G. KRAINICK, Arch. f. Kinderh. **110**:24, 1937.

Two cases of encephalitis with measles are reported. The first case is of interest because of the unusually early appearance of the nervous complications. The second case is unusual because of the associated onset of menstrual bleeding in a sexually undeveloped child.

The genesis of encephalitis in measles and other encephalitides associated with or following infections is discussed in the light of recent biologic and histopathologic observations.

CRANE, Washington, D. C.

FAMILIAL DISPOSITION TO NEPHRITIS IN SCARLET FEVER. F. SCHURICHT, Kinderärztl. Praxis **7**:539 (Dec.) 1936.

Schuricht observed eleven siblings, seven of whom contracted scarlet fever. Six of the seven had nephritis, three with uremia. The author believes that the occurrence of nephritis in six members of one family is explained by the existence of a familial disposition to nephritis.

HEYMANN, Cleveland.

APPLICATION OF MALARIA TREATMENT FOLLOWING THE STAGE OF ACUTE PARALYSIS IN EPIDEMIC POLIOMYELITIS. O. KAUDERS, Med. Klin. **32**:1766 (Dec. 24) 1936.

The article is a conclusion to one appearing in the preceding number of the same journal. Malaria treatment of three patients with poliomyelitis accompanied with rather extensive paralysis is reported. Treatment was begun on the thirty-fourth, the forty-fifth and the fifty-second day, respectively, after the onset of the illness, and the patients were permitted to have seven, ten and nine attacks,

respectively, of fever. Considerable clinical improvement in the paralysis was noted soon after termination of the treatment. The spinal fluid also showed improvement. Muscle mass and electrical reactions were not improved. The optimum time for malaria treatment is as yet undetermined. Although the report is preliminary and although the author admits that further study is necessary, he feels justified in stating that malaria treatment has become an important therapeutic aid in combating the severe residual paralyses.

SIEMSEN, Chicago.

THE FACIAL PHENOMENON IN DIPHTHERIA. H. RAVE, Monatschr. f. Kinderh. **69**:73 (Feb.) 1937.

Some writers have noticed the occurrence of a facial phenomenon in diphtheria. To determine how frequently this Chvostek sign develops and the effect on it of subsequent diphtheria, Rave examined over 9,000 school children. Unfortunately for his study, only 20 of them later had diphtheria. From a study of these he draws certain conclusions:

1. When the facial phenomenon exists as a sign of a congenitally abnormal nervous system, it usually disappears in the first six to twelve days of a diphtheritic infection and reappears subsequently.

2. The diphtheria toxin in certain cases does not involve the facial nerve, as in some of these patients the phenomenon remained uninfluenced by the disease.

3. Diphtheria toxin caused increased irritability of the facial nerve in some of the group who did not show the sign as well as in some of those in whom the sign was demonstrated before the onset of the disease.

GERSTLEY, Chicago.

TYPES OF DIPHTHERIA BACILLI. WENZEL BECKER, Monatschr. f. Kinderh. **69**:95 (Feb.) 1937.

In the Leipzig children's hospital 137 strains of diphtheria organisms from 100 patients were grouped. It was found that 64 per cent belonged to the malignant type, 20 per cent to the intermediate, and 16 per cent to the mild. However, each type is capable of producing serious and even fatal disease.

GERSTLEY, Chicago.

MEASLES PROPHYLAXIS AND PLACENTAL EXTRACT. U. MOELLER, Monatschr. f. Kinderh. **69**:101 (Feb.) 1937.

Of ninety-one children incubating measles, who were aged from 3 months to 5 years, forty-four were treated by injections of placental extract in doses of from 3 to 20 cc. on the fifth to seventh day of incubation. Of these, thirty-five came down with measles, a protection of only 20 per cent. Forty-seven children were given from 10 to 15 cc. on the second day of incubation, with a protection of 97 per cent.

GERSTLEY, Chicago.

TREATMENT OF MEASLES. K. OXENIUS, München. med. Wchnschr. **84**:293 (Feb. 19) 1937.

Oxenius gives some interesting statistics relating to measles in Chemnitz during the last thirty-five years. During that period there were 868 deaths from measles, 97 per cent in children under 5 years of age. There has been an almost steady decrease in the mortality during the last twenty years—from a maximum of 60 deaths per year to 6 deaths in 1935. Oxenius recalls that twenty-seven years ago Czerny stated that if children were properly nourished the infectious diseases would be less dangerous. This statement amused the younger assistants at that time (including Oxenius), but today Czerny's prophecy has been verified. Oxenius finds that children who are overweight and are fed as were all children a few decades ago do not withstand infectious diseases as well as their better nourished playmates.

This speaks against attenuation of the measles virus. The mortality rate from other infectious diseases has also decreased. Comparing a sixteen year period before 1918 with a similar period after that date, it is found that the mortality rates from scarlet fever, pertussis and diphtheria have decreased about 75 per cent.

Better resistance has decreased the complications in measles, and hence the treatment can be simplified. Rest in bed is necessary only for the duration of the rash. Light is excluded only when it causes discomfort to the patient. Quinine therapy has decreased the mortality from pneumonia.

BRAHDY, Mount Vernon, N. Y.

RESULTS OF CULTURES TAKEN EVERY TWO HOURS IN CASES OF DIPHTHERIA AND DIPHTHERIA CARRIERS. E. LENZ, München. med. Wchnschr. **84**:698 (April 30) 1937.

Lenz took nose and throat cultures every two hours between 6 a. m. and 8 p. m. from seventy-two patients with clinical diphtheria and seventeen diphtheria carriers. She found that the morning cultures were positive for Klebs-Löffler bacilli from 40 to 50 per cent more often than the afternoon cultures. In addition she studied the therapeutic value of the topical application of lemon juice in diphtheria carriers. Lemon juice failed to retard the growth of diphtheria bacilli.

BRAHDY, Mount Vernon, N. Y.

WHAT MAY THE PRACTITIONER EXPECT FROM THE BACTERIOLOGIC EXAMINATION IN SUSPECTED CASES OF DIPHTHERIA? P. DAHR, München. med. Wchnschr. **84**:700 (April 30) 1937.

According to Kleinschmidt, 20 per cent of the initial cultures in clinical diphtheria are negative. Unfortunately many physicians have a false impression as to the significance of the bacteriologic report in a case suspected of being one of diphtheria. The diagnosis of diphtheria should be established by the clinician, not by the laboratory. When diphtheria is suspected, it is much more important to reach for the serum syringe than for the culture tube. Today it is known that the therapeutic failure of diphtheria serum is the result of giving it too late in the disease.

BRAHDY, Mount Vernon, N. Y.

DETOXIFYING DIPHTHERIA TOXIN WITH STEARINES. M. EISLER and F. GOTTDENKER, Wien. klin. Wchnschr. **50**:54 (Jan. 15) 1937.

Some time ago Ramon and co-workers reported that the immunizing power of diphtheria and tetanus formaldehyde toxoids can be increased by addition of various complements—for example, hydrous wool fat or olive oil—and that, besides stimulating production of antitoxin in the body, these stearines cause detoxication of the poison itself.

Eisler and Gottdenker have investigated further the question of how the stearines work. Using cholesterol as one of the complements, they made the following observations: (1) If the antigen was not mixed with cholesterol but instead the latter was given to a test animal intraperitoneally twenty-four hours before subcutaneous injection of the toxoid, stimulation of the antibodies failed completely. (2) If cholesterol was mixed with the toxoid or toxin in amounts sufficient to accomplish detoxication, this mixture, when injected, raised production of antibodies remarkably. (3) If the cholesterol-toxin mixture was dissolved in benzine and this solution shaken with water, the results after injection were the same as with the toxoid alone.

ABT, Chicago.

PARALYSIS OF THE PLEXUS BRACHIALIS DURING POSTDIPHTHERIAL POLYNEURITIS M. REGER, Wien. klin. Wchnschr. **50**:162 (Feb. 5) 1937.

The relation between diphtheria and the nervous system is well known. The disease is frequently followed by various forms of paralysis—e. g., facial paresis,

oculomotor paralysis in the form of ptosis, and paralysis of the extremities. Reger reports a unique case of marked paralysis in the musculature of the shoulder girdle due to paralysis of the brachial plexus.

A 14 year old girl, during convalescence from diphtheria gravis, at the beginning of the seventh week began to experience paresthesia in her hands, though motility, sensibility and the reflexes remained normal. Four days later, however, symptoms of polyneuritis appeared, including difficulty in swallowing and speaking. In the course of the next week, ataxia and involvement of the shoulder musculature became apparent. Although the motor power of the hands remained unimpaired, there was evident ataxia in the finger to finger and the finger to nose test, and the patient had great difficulty in raising her arms and felt severe paresthesia in doing so. The eyes were also affected; accommodation was disturbed, and there was double vision.

After ten days the throat manifestations began to disappear, and twenty days later the girl's speech had become normal and her general condition much improved; she could stand, the ataxia had moderated, and movements of the arms were easily performed.

Three months after discharge there were no pathologic conditions to be found except mild paresthesia of the extremities.

ABT, Chicago.

CARDIAC CHANGES IN PERTUSSIS. N. MORIGUCHI, Acta pædiat. japon. **43**:1 (Jan.) 1937.

Moriguchi summarizes the observations at autopsy as to cardiac changes in twenty-two children who died of pertussis, as follows: (1) The cardiac enlargement so often observed in such children cannot be interpreted as being directly due to the pertussis, since so many show complicating pneumonia, which may be the underlying cause. (2) Roentgenographic examination of the heart reveals what is called "pertussis heart," which is characterized by generally diminished height with displacement of the apex to the left so that the cardiophrenic angle becomes obtuse. This together with the dilatation of the right ventricle causes the lateral diameter of the heart along the diaphragm to be greatly increased. The author likens this peculiarity in the cardiac shadow to a soft water bag sitting on a sphere and considers it to be highly characteristic of pertussis.

KATO, Chicago.

EPIDEMIOLOGICAL NOTES ON SCARLET FEVER IN CHINA. H. S. GEAR, Chinese M. J. **51**:203 (Feb.) 1937.

It is evident that scarlet fever has a modern origin in China, for until 1902 the infection was practically unknown there. In that year there were 1,500 Chinese with the disease.

The writer gathers his records from a survey of sixteen hospitals in 1933 and twenty-five in 1934, accounting for 248 patients. The disease is now widely distributed in China and attacks chiefly adolescents, rather than younger children, in urban communities.

NEFF, Kansas City, Mo.

POST-VACCINAL EXANTHEMA. T. AKIYAMA, J. Orient. Med. **26**:13 (Jan.) 1937.

Akiyama reports eight cases of postvaccinal exanthema, seven of which were in infants under 1 year of age and the last in an 8 year old girl. In all infants the exanthema occurred following the first vaccination, and in the older child, after the second vaccination. The eruptions appeared from six to twenty days after vaccination and consisted of vesicular red nodules, and in three cases pustules were also present. The face and extremities were mostly affected. The mucous membranes were free in every case.

KATO, Chicago.

SCARLET FEVER AND RHEUMATISM. P. H. KRAMER, Nederl. tijdschr. v. geneesk. **81**:355 (Jan. 23) 1937.

In two girls 9 and 15 years old scarlet fever was followed by inflammation of joints, endocarditis and chorea. Kramer is of the opinion that some of the arthritides after scarlet fever have a specific character and are caused by a secondary infection with the virus of acute rheumatism. He stresses the varying occurrence of rheumatism and endocarditis in epidemics of scarlet fever and pleads in favor of the application of large quantities of salicyl in such cases. The characteristic rheumatic nodules of Aschoff were found in some cases of scarlet fever complicated by rheumatism.

VAN CREVELD, Amsterdam, Netherlands.

PUSTULOSIS VARIOLIFORMIS SEU VACCINIFORMIS ACUTA. R. KOOIJ, Nederl. tijdsch. v. geneesk. **81**:571 (Feb. 6) 1937.

This is the record of a fatal case of pustulosis varioliformis seu vacciniformis acuta in a boy of 7 months. No contact with children recently vaccinated against smallpox could be proved. Inoculation of the splenic pulp in the cornea of a rabbit failed to produce Guarnieri's bodies.

VAN CREVELD, Amsterdam, Netherlands.

## Acute Infectious Diseases

INDEPENDENCE OF CHOREA AND RHEUMATIC ACTIVITY. A. F. COBURN and L. V. MOORE, Am. J. M. Sc. **193**:1 (Jan.) 1937.

Coburn and Moore quote Gerstley, who stated that chorea without other rheumatic manifestations should not be taken as an indication of rheumatic infection. The authors' original group of rheumatic patients included ten persons who had chorea apparently unrelated to rheumatic activity—none of whom presented any other manifestation of rheumatic disease in a subsequent five year period. In one half of the cases under observation, chorea occurred in nonrheumatic subjects, in one fourth it occurred in quiescent rheumatic subjects and in about one fourth it occurred in persons who were actively rheumatic. Normal blood sedimentation rates accompany uncomplicated chorea.

HENSKE, Omaha.

CLINICAL STUDIES ON HUMAN LUNG FLUKE DISEASE (ENDEMIC HEMOPTYSIS CAUSED BY PARAGONIMUS WESTERMANI INFESTATION. Z. BERCOVITZ, Am. J. Trop. Med. **17**:101 (Jan.) 1937.

Bercovitz briefly reviews the literature on this subject and then reports the result of two years of study of this disease in Korea. He states that patients with pulmonary distomiasis are not particularly predisposed to tuberculosis. The conditions may coexist, but such coexistence is uncommon.

The age of incidence is from 8 to 64 years, with a duration of from one month to twenty years. The sputum resembles that of a patient with tuberculosis. In the case of children who swallow their sputum, the ova are found in the stools. There is no typical blood picture and neither is the x-ray picture of the chest characteristic.

The treatment of patients with endemic hemoptysis is unsatisfactory, as there is no known specific drug. Emetine hydrochloride is used, but no cures are recorded, though many seemed improved.

BURPEE, Augusta, Ga.

FULMINATING SEPTICEMIA ASSOCIATED WITH PURPURA AND BILATERAL ADRENAL HEMORRHAGE (WATERHOUSE-FRIDERICHSEN SYNDROME): REPORT OF TWO CASES WITH REVIEW OF THE LITERATURE. M. S. SACKS, Ann. Int. Med. **10**:1105 (Feb.) 1937.

The cases of a white girl aged 4 years and another aged 2½ years formed the basis of this report. A necropsy was performed in each instance. Sacks

considered the picture in these cases sufficiently definite to justify the classification of this syndrome as a clinical entity.

The etiology and pathology were discussed. A review of the literature showed that in 60 per cent of the reported cases the disease was meningococcic in origin, while in 40 per cent it was due either to Streptococcus haemolyticus or to Pneumococcus. The outstanding pathologic change was bilateral adrenal hemorrhage, usually massive. The clinical picture was that of purpura associated with severe sepsis.

READING, Galveston, Texas.

STREPTOCOCCUS HAEMOLYTICUS BACTEREMIA. G. SCHWARTZMAN and J. L. GOLDMAN, Arch. Surg. **34**:82 (Jan.) 1937.

This study is concerned with an analysis of 168 cases occurring within a period of five and a half years. In all of the cases blood cultures revealed Streptococcus haemolyticus bacteremia. The mortality rate for the entire group was 54 per cent. The highest mortality rate, from 60 to 100 per cent, was encountered in cases of the following conditions: gynecological infections, articular and osseous infections, surgical postoperative infections, pulmonary infections and acute otitis media with meningitis. In cases of secondary erysipelas the mortality rate was 20 per cent; in those of infections of the upper respiratory tract, 34 per cent; in those of peripheral infections, 36 per cent.

The authors concluded that a quantitative estimation of the number of hemolytic streptococci in the blood stream had both diagnostic and prognostic significance. In the groups in which the mortality was relatively low there was a high percentage of positive blood cultures in fluid mediums only, while in the groups with relatively high mortality there was a high percentage of such cultures in both solid and fluid mediums.

KAISER, Rochester, N. Y.

SERUM THERAPY IN HUMAN BRUCELLOSIS. L. FOSHAY, J. Bact. **33**:42 (Jan.) 1937.

Foshay believes that in terms of therapy the distinction between acute and chronic brucellosis in man is drawn arbitrarily at the end of the seventh month of disease. On this basis antiserum is given for the acute condition. He treated seventy-seven consecutive patients for the acute condition. Fifty-four patients received goat serum; twenty-one received horse serum. No differences attributable to the difference in animal source were noted. No patient failed to make a permanent recovery. The average duration of the disease to the time of the administration of serum was seven and six-tenths weeks (minimum one week, maximum twenty-nine weeks). The average duration of fever after the institution of serum therapy was sixteen days (minimum less than one day, maximum ninety days). The average duration of symptoms after the beginning of serum treatment was twenty-nine days (minimum less than one day, maximum seven months). The average period of disability after serum was started was one and seven-tenths months (minimum zero, maximum nine months). The average total duration of disease was three and nine-tenths months (minimum one and two-tenths months, maximum eleven months).

STOESSER, Minneapolis.

OBSERVATIONS ON THE EFFECT OF PRONTOSIL AND A RELATED COMPOUND IN HEMOLYTIC STREPTOCOCCUS INFECTIONS. P. GROSS, F. B. COOPER and R. R. MELLON, J. Bact. **33**:72 (Jan.) 1937.

The observation has been made by other investigators that the protective and curative effect in mice of a new derivative of sulfanilamide (para-aminobenzenesulfonamide base) known as prontosil soluble (the disodium salt of 4′-sulfamidophenyl-2-220-7-acetylamino-1-hydroxynaphthalene-3, 6-disulfonic acid) discloses a remarkable paradox. Mice infected with highly virulent mouse passage strains of human origin showed a much higher percentage of recovery than mice infected with nonpassage human strains of low virulence. Realizing the effect of strain diversity in mice, the authors thought repetition with other strains desirable.

Accordingly, the Pion strain (Pasteur Institute) of relatively low virulence and the Stoddard strain, human type, of high virulence were employed. Although definitely favorable effects were noted with the Stoddard strain, no comparison can as yet be drawn between it and the Pion, owing to an unexpected fluctuation in virulence that occurred in the Stoddard strain. But with the Pion strain only one of ten controls was alive after fifteen days, while six of the treated mice were alive and apparently normal. Similar results were obtained with the already known sulfanilamide.

In several clinical cases a favorable effect appeared, but in only one—a case of meningitis due to a hemolytic streptococcus—was it of high evidential value. No final conclusions can be drawn.

STOESSER, Minneapolis.

EXPERIMENTAL RABIES IN WHITE MICE: II. STUDIES ON PASSIVE IMMUNIZATION. A. HOYT, R. T. FISK, F. J. MOORE and R. L. TRACY, J. Infect. Dis. **59**:152 (Sept.-Oct.) 1936.

These authors found that if these were intraperitoneal injections of antiserum a short time before intracerebral injections of virus, a higher percentage (36 per cent) of the mice thus treated survived than was observed among the controls (9 per cent). Antiserum injected sixteen days before, or shortly after, the virus was given was ineffective, as was normal serum and serum prepared against normal rabbit brain. Antiserum injected intracerebrally was effective one-half hour before, but not twenty-four hours before or two hours after virus was injected intracerebrally. Antiserum injected intraperitoneally four days or less before the intramuscular injection of virus protected, as did antiserum given one day after the injection of virus.

In short, these experiments illustrate the difference in results obtained when different avenues of entrance are employed. They also illustrate the importance of the portal of entry in this disease.

TOOMEY, Cleveland.

TYPHOID FEVER IN CHILDREN: A STUDY OF SIXTY CASES. H. F. DIETRICH, J. Pediat. **10**:191 (Feb.) 1937.

An analysis was made of sixty cases of typhoid fever in the Children's Hospital, Boston. The outstanding features of this analysis as given in the author's summary are:

"1. Abdominal pain is prominent at the onset of 50 per cent of cases.

"2. The white count may be high during the early stage of the disease; the leucopenia apparently appears just after the blood stream is invaded.

"3. The appearance of typhoid bacilli in the stools occurs with great irregularity in single cases.

"4. The Widal is positive by the end of the second week in 60 per cent of the cases.

"5. The disease in children is characterized by an abrupt onset, frequent appearance of neurologic symptoms, a shorter course, and lower mortality rate than is found in adults.

"6. The complications are largely pyogenic; hemorrhage and perforations are rare, presumably due to the superficial character of the intestinal ulcerations.

"7. In the majority of sporadic cases the source could not be determined."

RAUH, Cincinnati.

A CASE REPORT OF THE EASTERN TYPE OF ROCKY MOUNTAIN SPOTTED FEVER. J. H. STOKES, J. South Carolina M. A. **33**:27 (Feb.) 1937.

The Eastern type is less virulent and develops later in the season. It is usually transmitted by the common dog tick, Dermacentor variabilis.

WESTON JR., Columbia, S. C.

TREND OF PREVENTION, THERAPY AND EPIDEMIOLOGY OF DYSENTERY SINCE THE DISCOVERY OF ITS CAUSATIVE ORGANISM. K. SHIGA, New England J. Med. **215**:1025 (Dec. 24) 1936.

Shiga suggests the following classification of causative factors:

1. Bacillus dysenteriae (a representative strain is the Shiga-Kruse bacillus); it includes toxin-producing, nonmannitol-fermenting organisms.

2. Bacillus metadysenteriae (representative strains are the Flexner, Strong Y, Ohno and Schmitz); it includes mannitol-fermenting, nontoxin-producing organisms.

3. Bacillus paradysenteriae (representative strains are the Kruse-Sonne and the Ohara-Mita); it includes lactose-fermenting, milk-coagulating and variant colony-forming organisms). Included in this group is the bacillus which causes Ekiri.

Ekiri (perhaps similar to the so-called summer diarrhea of children in the United States) in particular has been regarded as the most dreaded disease of children from its fulminating course and very high mortality. It begins with a sudden high fever and is followed immediately by convulsions and vomiting, and within from twenty-four to forty-eight hours from the onset the disease is fatal. Children of from 4 to 6 years old are especially subject to the disease, and the mortality is as high as from 70 to 80 per cent. The causative organism of ekiri is known as the Ohara-Mita bacillus. Later it was proved to be identical with an organism described by Sonne in 1915.

It was found that the dysentery antitoxin was especially effective in the treatment of patients with mild and moderate dysentery, but for those whose dysentery was severe it was less effective. The reason why it was not effective may have been that dysentery toxin acts on the peristaltic centers of the intestinal walls and that when paralysis of the intestinal walls has set in the antitoxin has no power to neutralize the toxin. The serum treatment is not effective in metadysentery and paradysentery. In recent years the Shiga type has practically disappeared, while the paradysentery bacillus has begun to appear in Japan.

Why has the dysentery bacillus been replaced by the metadysentery and paradysentery bacilli? One may surmise that the number of cases in which the dysentery bacillus is involved is small because its carriers are few, and likewise that the number of cases of metadysentery and of paradysentery is large because the number of their carriers is large.

Shiga believes that suppression of intestinal infectious diseases like typhoid and dysentery must rely on the progress of modern public health practices.

Oral vaccination has been administered in Japan to hundreds of thousands of people during the last ten years. Though the results are claimed to be statistically favorable, careful consideration is needed before they are accepted.

GENGENBACH, Denver.

INCREASING IMPORTANCE OF UNDULANT FEVER. J. KOGAN, New York State J. Med. **36**:1653 (Nov. 1) 1936.

Of six cases reported, three were in children. Tests by the use of the Huddleson antigen may be made at the bedside.

AIKMAN, Rochester, N. Y.

CHRONIC MENINGITIS IN WEIL'S DISEASE. F. MURGATROYD, Brit. M. J. **1**:7 (Jan. 2) 1937.

Murgatroyd reports an interesting case of Weil's disease associated with chronic meningitis. The report does not lend itself to abstraction. Treatment was by repeated lumbar punctures. On occasion a culture disclosed Leptospira icterohaemorrhagiae. All other examinations of the spinal fluid were negative so far as direct examinations went. But on injection of the spinal fluid into an animal, the animal died of infection with this organism, which was recovered at autopsy. Of special interest was the very late onset of the meningitis, which was of an insidious nature, and the prolonged course, the disease becoming chronic eventually.

ROYSTER, University, Va.

THE NOSE AND THROAT IN RELATION TO THE RHEUMATIC DISEASES. H. BARWELL, Lancet **1**:67 (Jan. 9) 1937.

When a sore throat has been followed by rheumatic fever it is proper, according to Barwell, that the tonsils should be removed. Numerous smaller nodules of lymphoid tissue remain scattered over the pharynx, so that acute pharyngitis can and does occur after tonsillectomy. Hence this operation does not with certainty prevent recurrence of acute rheumatism, though it makes it less probable.

Diagnosis of tonsillar sepsis is easy in many cases but difficult in others, and as usual it is more difficult to exclude the diagnosis of an unhealthy condition than to confirm it. Redness of the anterior pillar is considered an important sign. Squeezing the tonsil after cocainization or aspirating it with a suction cup may give valuable evidence.

LANGMANN, New York.

HYDATID DISEASE IN CHILDREN. H. B. GRAHAM, M. J. Australia **1**:206 (Feb. 6) 1937.

During the past thirty-six years 151 children have been admitted to the Children's Hospital, Melbourne, with hydatid disease. The histories of 74 children admitted since 1910 have formed the basis for the present study. There was a yearly average of 7.4 patients in the first ten years of the period under review, but since 1930 the yearly average has fallen to 2.2 patients. This steady decrease in the incidence of the disease probably has resulted from hygienic regulations at slaughter yards, education of the general public and improvement in medical and surgical practice. The incidence of the disease was fairly evenly distributed between the ages of 4 and 14 years except for 30 per cent of the 74 cases occurring between 6 and 7½ years of age. Simple hepatic cysts were more common in children over 7½ years of age and multiple cysts of the liver, pulmonary cysts and cysts in both the liver and the lung were more prevalent under that age. Daughter cyst formation was present in only 12 of the children. The view that rupture of the cyst precedes and causes the infection which leads to suppuration is supported. The relative value of diagnostic tests (Casoni intradermal test, precipitin test and complement fixation test) is discussed. In general, serum in the cases studied has failed to fix complement in uncomplicated cases but after leakage of antigen from the cyst to the host, resulting from rupture, onset of infection or operative intervention, the amount of complement fixed has risen considerably. The outstanding value of roentgenography is taken for granted. There were only 9 deaths among the 74 patients. With pulmonary and hepatic cysts the prognosis for the survival of the patient is good, even when rupture and suppuration have occurred, provided that the patient is over 4 years of age. With cysts in other sites the factor of age increases the likelihood that a cyst will show up in a vital spot during childhood, and there is usually some indication to modify the favorable prognosis when necessary. Special reference is made to pulmonary cysts and cysts of the brain, rather than to hepatic cysts, because of the relative importance of the former sites in childhood, and a series of case histories is included to show the clinical features of infestation in unusual sites.

GONCE, Madison, Wis.

AGGLUTINISM OF TYPHOID CARRIERS. A. PIJPER and C. G. CROCKER, South African M. J. **11**:113 (Feb. 27) 1937.

In their search for typhoid carriers the authors have always limited their cultural investigations to persons who possess appreciable quantities of O agglutinins, but recent experience seems to show that Vi agglutination would provide a better method of narrowing the field for cultural examinations.

GONCE, Madison, Wis.

CLINICAL AND BACTERIOLOGIC STUDY OF TYPHOID IN INFANCY. A. NACCARI, Pediatria **45**:33 (Jan.) 1937.

Naccari conducted a clinical and bacteriologic study on thirty-seven cases of typhoid infection in children ranging in age from 14 months to 12 years. He isolated in 59.4 per cent of the cases bacilli of type I, in 16.2 per cent bacilli of type II, in 8.1 per cent bacilli of paratyphoid type A and in 16.2 per cent bacilli of paratyphoid type B.

Those classifications were based on the behavior of the germ with respect to xylose and arabinose according to Jakobsen, Hieling and Stern. Regarding the clinical forms produced by them, no particular difference of virulency between the strains of type I and those of type II has been noted, both giving rise to severe disease, while the groups paratyphoid A and B have both given prevalence to disease of a serious type.

PALMIERI, Brooklyn.

TREATMENT OF BACILLARY DYSENTERY. E. DIAZ ORERO, Arch. de med. inf. **6**:134 (March) 1937.

Active dysentery should be treated with specific serum and venoclysis. In times of epidemics fruits should be forbidden. At other times raw fruits and vegetables should be well washed, and milk and water, boiled.

SANFORD, Chicago.

OBSERVATIONS ON TWENTY-TWO CASES OF TETANUS. D. ADERALDO CHAVES, Arch. de pediat., Rio de Janeiro **9**:103 (Jan.) 1937.

An excellent article is this on the symptoms and course of tetanus. It is well illustrated with photographs. The author believes that 5,000 units should always be used for prophylaxis.

SANFORD, Chicago.

TREATMENT OF ERYSIPELAS IN INFANCY WITH A DERIVATIVE OF SULFANILAMIDE, PRONTOSIL SOLUBLE (THE DISODIUM SALT OF 4′-SULFAMIDOPHENYL-2-220-7-ACETYLAMINO-1-HYDROXYNAPHTHALENE-3, 6-DISULFONIC ACID). M. GARCIA and D. PILLAR, J. de pediat., Rio de Janeiro **4**:71 (Feb.) 1937.

The authors used injections of this drug in two cases of erysipelas. The infants were 11 and 4 months of age. They recovered promptly.

SANFORD, Chicago.

INFLUENCE OF VITAMIN A ON THF BACTERICIDAL POWER OF WHOLE BLOOD IN CHILDREN WITH VARIOUS INFECTIOUS DISEASES. G. MELODIA, Med. inf. **8**:5 (Jan.) 1937.

Observations were made on the bactericidal power of the blood against the staphylococcus and the colon bacillus. Two of the ten children had staphylococcic infections of the skin, one bacillary dysentery, one disseminated bronchopneumonia and six pyelocystitis. The method of Lusena was used. Observations were made before and from five to ten days after the administration of 500 international units (equivalent to U. S. P. units) of vitamin A. The giving of vitamin A led to varying results, some children showing increase, some no change and others decrease in hematic bactericidal power. Melodia concluded that vitamin A was of value in increasing the bactericidal power of the blood only in those children who had had an insufficient amount of that vitamin.

HIGGINS, Boston.

LATENT RHEUMATISM OF THE NERVOUS SYSTEM IN CHILDREN. R. MILNER, Monatschr. f. Kinderh. **69**:108 (Feb.) 1937.

In an unnecessarily verbose article, the writer airs his views on rheumatism, based largely on observations of others and not supported by experimental evidence. He believes that rheumatism is the result of an allergic condition of the mesenchyme, which is hypersensitive as a result of frequent infections or exposures to cold, and is activated by a renewed exposure to the antigen. The various neuralgias and myalgias are simply manifestations of the general condition and warnings of an underlying rheumatic process. Females are more frequently affected than males owing to the insufficient clothing dictated by popular fashion.

GERSTLEY, Chicago.

PARASITIC INFESTATION OF EGYPTIAN INFANTS AND CHILDREN. A. KHALIL ABDEL KHALIK, J. Egyptian M. A. **20**:9 (Jan.) 1937.

The stools of seventy-two children admitted to a hospital for illness and of forty-six well infants in a foundling's home were examined, and sixty-one (or 51.7 per cent) of these children were found to have intestinal parasitic infestation. Eosinophilia was the most important blood modification. Some parasites (Ankylostoma) gave high eosinophilia, others gave moderate eosinophilia, while in some of the blood pictures this feature was absent. Of twenty-five children not infested, 72 per cent had a hemoglobin estimation below 65 per cent, while, of 21 infested, the hemoglobin of 81 per cent was below this figure.

MULHERIN, Augusta, Ga.

INCIDENCE OF HELMINTHIC PARASITES WITH SPECIAL REFERENCE TO THE EPIDEMIOLOGY OF FASCIOLOPSIS BUSKII IN SHIAOSHAN, CHEKIANG, 1934-1935. J. Y. C. WATT, Chinese M. J. **51**:77 (Jan.) 1937.

In a survey of the area mentioned, the percentage of helminthic infestation was 83.84 for Fasciolopsis buskii, 38.04 for Ascaris, 12.32 for Trichocephalus and 0.89 for hookworm. The occurrence of Fasciolopsis buskii is more common in children and in males.

NEFF, Kansas City, Mo.

MENINGITIS IN COURSE OF WEIL'S DISEASE CAUSED BY LEPTOSPIRA CANICULA. C. J. ROOS, Nederl. tijdschr. v. geneesk. **81**:33 (Jan. 2) 1937.

A woman of 23 years had symptoms of the meningeal form of Weil's disease and changes in the spinal fluid, which proved to be caused by Leptospira canicula. The same leptospira could be cultured from the patient's urine and from the patient's dog.

VAN CREVELD, Amsterdam, Netherlands.

ACTION OF METHYLTHIONINE CHLORIDE ON AVIAN MALARIA. I. C. ALBRICHT and C. NIEUWENHUYSE, Nederl. tijdschr. v. geneesk. **81**:483 (Jan. 30) 1937.

Opinions differ as regards the action of methylthionine chloride on the different forms of malaria parasites occurring in man. The authors studied the question experimentally once more. They found that this drug acts only on Plasmodium relictum (canary malaria). It has most marked action on Haemoproteus orizivorae (rice-bird malaria), so it has a pronounced action on gametes. It is striking that when injected intramuscularly it is much more effective than when administered orally.

In combination with methylthionine chloride, quinine shows markedly increased action on P. relictum. This justifies, from the authors' point of view, further clinical investigation with methylthionine chloride in combination with quinine or in connection with a quinine cure, in which methylthionine chloride should be injected intramuscularly or perhaps rectally.

VAN CREVELD, Amsterdam, Netherlands.

## Chronic Infectious Diseases

EXPERIMENTAL STUDY OF CONGENITAL SYPHILIS, INCLUDING A STUDY OF THE INFECTIOUSNESS OF BLOOD, UTERUS AND PLACENTA OF PREGNANT RABBITS WITH EARLY SYPHILIS. J. E. KEMP and P. D. ROSAHN, Bull. Johns Hopkins Hosp. **60**:45 (Jan.) 1937.

Spirochetes were inoculated in granulating wounds on the backs of female rabbits and infections proved by dark field examination of serum from the lesions at the sites of inoculation. In five of these animals spirochetes were demonstrated in the blood and placentas before term, and since all animals were treated the same way it was assumed that spirochetes were present in the blood at term in the remaining animals. An organ emulsion of forty-seven fetuses, the offspring of twelve mothers, failed to infect normal rabbits, from which it is concluded that either the placenta forms a barrier to the spread of infection from the syphilitic female rabbit to her offspring or the spirochetes are destroyed after reaching the fetus. The latter conclusion is not considered likely by the authors. There was no difference in susceptibility to infection between the offspring of normal and those of syphilitic mothers.

LYTTLE, New York.

EFFECT OF PREGNANCY AND OF FEMALE SEX HORMONES IN MODIFYING THE COURSE OF SYPHILIS IN EXPERIMENTAL ANIMALS. J. E. KEMP, J. Infect. Dis. **60**:32 (Jan.-Feb.) 1937.

Although the number of animals involved in this experiment is small, and the results are not absolutely convincing, it is nevertheless suggested by this and other experimental and clinical studies that while pregnancy exerts an appreciable inhibiting effect on the course of syphilitic infection, it is not the only factor responsible for alteration in the course of the disease in the female. The experiences of Frazier and his colleagues in the treatment of experimental syphilis in rabbits with an estrogenic substance prepared from the urine of pregnant women suggest that estrogen might be responsible for the modified course of the infection in the pregnant female. Kemp's findings are not in agreement with theirs. Whether this is because the material they used contained a larger amount of estrogenic substance than that used by Kemp, or because the latter's material contained, in addition, an appreciable quantity of gonadotropic hormone or other substances, is not evident at present. It is evident, however, that further experimental and clinical studies are necessary before the relationship of sex and pregnancy to the course of syphilitic infection can be accurately determined.

TOOMEY, Cleveland.

SURVIVAL OF OXYGEN AND WATER DEPRIVAL BY TUBERCLE BACILLI. T. S. POTTER, J. Infect. Dis. **60**:88 (Jan.-Feb.) 1937.

"For the present the statement is best made, that the severest deprival of oxygen and water yet accomplished does not guarantee the death of tubercle bacilli, but that under such conditions the bacilli in substantial numbers retain their viability. In fact the avian bacilli subjected to such conditions, at body temperature, for more than a year, consistently survive in substantial numbers; at room temperature they survive for at least two years."

TOOMEY, Cleveland.

SYPHILIS AND PREGNANCY. S. D. SOULE, J. Missouri M. A. **34**:84 (March) 1937.

In the Washington University Clinic, obstetric division, there were 4,700 admissions from Nov. 1, 1931, to Jan. 1, 1936.

Syphilis was present in 109 of the 3,245 white women (3.35 per cent) and in 213 of the 1,455 Negro women (14.64 per cent) admitted during this period. The general incidence of syphilis in the entire obstetrical clinic was 6.85 per cent. Only 189 patients from this group received treatment and were available for study.

A careful history of known infection in the patient or in the husband is taken on admission, and a Wassermann test is made. From these results the condition of the patient is classified as negative, doubtful or positive. Treatment is instituted on this basis.

At the time of delivery a Wassermann test is made on the mother's blood and on the blood of the umbilical cord. Another Wassermann test is made, when possible, on the infant's blood at 3 months of age.

Treatment is recommended in all cases in which a doubtful diagnosis is made, and in all cases in which the Wassermann reaction is positive, treatment is begun as soon as the diagnosis is made and continued without intermission until pregnancy is terminated. Weekly injections of arsphenamine or of neoarsphenamine are given for at least ten weeks, the last injection overlapping with a course of intramuscular injections of a bismuth preparation which are continued for from six to ten weeks. Then the arsenicals are again started. When inadequate time remains before delivery for such a course, the injections of the bismuth preparation are omitted.

In the group reported, only 10 patients received the maximum treatment (twenty or more consecutive weeks), with one neonatal death.

A close follow-up of the infant for at least three months, preferably for a year, is attempted.

The author makes the statement that "under our care patients who receive a moderate amount of treatment have almost a 95 per cent opportunity of delivering a living, normal, nonsyphilitic child."

BERGER, Kansas City, Mo.

THERMOTHERAPY IN EXPERIMENTAL TUBERCULOSIS. E. BOGEN, Proc. Soc. Exper. Biol. & Med. **36**:11 (Feb.) 1937.

In this investigation 225 guinea-pigs kept in forty-five cages at a temperature of over 80 F. (usually between 85 and 90 F.) for three months after inoculation with from 0.1 to 0.0001 mg. of virulent tubercle bacilli of the human type during the past five years showed on the average just half as much tuberculosis when necropsies were made at the end of three months as did 150 guinea-pigs similarly inoculated at the same time and kept in thirty cages at outside temperature. In only one set of guinea-pigs kept in a warm cage was more tuberculosis evident than in the controls, while forty-four sets of five guinea-pigs each kept in the warm cages showed less. The difference in the amount of tuberculosis found (the technic for determining the amount of tuberculosis present has been described previously [*Tr. Nat. Tuberc. A.* **28**:163, 1932]) was statistically significant whether the material was injected subcutaneously or inhaled. Previous studies have failed to show significant effects of darkness, ultraviolet rays, overcrowding, dampness or other environmental factors on the development of experimental tuberculosis in guinea-pigs. Reduction of the total caloric intake did not affect the conditions found in the animals. Administration of cod liver oil to the animals did not affect the results. The detrimental effects of feeding beryllium were exactly balanced by the beneficial effects of the warmth. There was no demonstrable increase in body temperature of these animals, and no changes in the leukocytes were observed, although the animals kept in the warmer environment showed better weight curves. The animals in the warm cages were quieter than the control animals thus the enforced intensive rest may be responsible for the beneficial results obtained.

HANSEN, Minneapolis.

CHRONIC MILIARY TUBERCULOSIS IN CHILDREN. R. H. FISH, Arch. Dis. Childhood **12**:1 (Feb.) 1937.

A series of ten cases of chronic miliary tuberculosis occurring in childhood is described. Recovery took place in four of these cases; microscopic sections of the lungs in three of the fatal examples demonstrated the healing process in indi-

vidual miliary nodules. The cases are discussed, and the following conclusions are reached:

1. Miliary tuberculosis is chronic more frequently than is generally recognized; recovery occurs in a fair proportion of the cases in which the disease is chronic.

2. Recovery is commonest when the nodules are confined to the lungs, but it may also take place when the disease is generalized and even when the onset of the illness is moderately acute.

3. The pathology in chronic and acute miliary tuberculosis is essentially the same.

4. Healing of individual miliary tubercles takes place by a process of fibrosis, which usually leads to their complete disappearance from the pulmonary roentgenograms.

5. Massive caseous glands in the upper mediastinum are a frequent finding in the juvenile type of chronic miliary tuberculosis; the presence of these glands may be responsible for the tendency to recurrent episodes of tuberculous bacillemia which is a feature of these cases.

6. Any one of these episodes may give rise to fatal meningitis; the risk of this complication occurring is, however, considerably diminished if strict rest in bed is maintained until the x-ray picture is clear.

KELLY, Milwaukee.

THE TECHNIC OF IMMUNIZATION AGAINST TUBERCULOSIS WITH B C G. B. WEILL-HALLÉ, Ann. méd.-chir. **1**:29 (Nov.) 1936.

Weill-Hallé feels that B C G is effective in preventing the development of tuberculosis if it is used under controlled conditions. He recommends subcutaneous injections in preference to ingestion and in his work used 0.04 mg. of the vaccine prepared by the Pasteur Institute. Each patient was inoculated in the first few days of life and then tested with tuberculin. If the tuberculin test was negative, the immunization was repeated in from six to twelve months. Local reactions were rare and insignificant, and even in infected persons no bad effects were observed. In the latter group, however, the immunization is futile. None of the subjects has yet succumbed to tuberculosis. If one is convinced of the value of B C G, the paper provides valuable suggestions as to the details of its administration.

DIETRICH, Los Angeles.

RÔLE OF THE BOVINE BACILLUS IN THE ETIOLOGY OF TUBERCULOUS MENINGITIS. E. LESNÉ, A. SAENZ, M. SALEMBIEZ and L. COSTIL, Arch. de méd. d. enf. **39**:798 (Dec.) 1936.

Little attention has been paid by French clinicians to the rôle that may be played by bovine tubercle bacilli in the production of tuberculous meningitis in children. In England and the Scandinavian countries, where raw milk is still used in infant nutrition, particularly in rural districts, intensive studies have been carried on.

In America, Park and Kunwiede (1910) and Gosling and Montanus (1924) have isolated bacilli of this type in 13.6 per cent of their cases; in Germany, Moellers found them in 6.9 per cent, and Lange, in 8.4 per cent; in the British Isles, Griffith, Griffith, Cobbett and Eastwood, between the years 1905 and 1931, reported numerous cases of bovine infection, the incidence varying from 25.5 to 40 per cent of the total number of cases of tuberculous meningitis.

The writers report an investigation at the Hospital Trousseau, conducted from 1932 to 1936, in which 138 cases were minutely examined. Using Löwenstein's culture medium for the spinal fluid, they were able to differentiate the bovine type of invasion in 9 instances, confirming their observations in all of these by inoculation of rabbits.

Inquiry brought out the fact that 8 of the children concerned had ingested raw milk over long periods; 7 of these were under 5 years of age. One had tuberculous antecedents, while of those infected by bacilli of the human type nearly all were exposed to family contagion.

AMESSE, Denver.

THE INITIAL STATES OF PRIMARY TUBERCULOUS INFECTION IN INFANTS. P. NOBÉCOURT, Gaz. d. hôp. **109**:1617 (Nov. 25) 1936.

This is a classroom lecture in which Nobécourt describes the commonly accepted views of the way of infection, the frequently symptomless course of even the severe infection and the grave prognosis.

In the last fourteen years every patient admitted to his hospital had a routine tuberculin test. Of those in the first three months of life 0.4 per cent, of those in the second three months 4.3 per cent, of those in the third three months 5.6 per cent and of those in the fourth three months 8.1 per cent, gave positive reactions. Of those between 1 and 1½ years 11.9 per cent, and of those between 1½ and 2 years 13.6 per cent, gave positive reactions.

While almost all of those under 1 year with positive reactions died, 16 per cent of the infants reacting positively in the second year were expected to recover. No follow-up of patients after discharge from the hospital is reported.

KAJDI, Baltimore.

TUBERCULOSIS IN 1937. P. LEREBOULLET and H. GAVOIS, Paris méd. **1**:1 (Jan. 2) 1937.

This is a review of the literature on tuberculosis appearing in the year 1937.

LESLIE, Evanston, Ill.

VACCINATION WITH BCG. R. CHAUSSINAND, Paris méd. **1**:15 (Jan. 2) 1937.

Chaussinand has vaccinated 617 infants with BCG, employing various modes of administration. He has followed most of these children through a period of several years and has never observed a single pathologic incident imputable to BCG. He also reports communications from five obstetricians in Saïgon who gave BCG to 60,000 new-born infants during the period from 1930 to 1936. These infants remained under observation for from eight to fifteen days, and no gastro-intestinal disturbance was noted which could be attributed to the ingestion of BCG. These clinical observations are strong evidence of the innocuousness of this vaccine.

LESLIE, Evanston, Ill.

SELECTION OF CONVALESCENT OR TUBERCULOUS CHILDREN. J. HUBER, Paris méd. **1**:22 (Jan. 2) 1937.

Huber feels that every child showing a positive tuberculin reaction should have a roentgen examination of the chest. If activity is shown either by the x-ray picture or by culture of the tubercle bacillus, the patient should be segregated. The child who has a history of exposure but who does not show a positive tuberculin reaction may associate with children whose tuberculosis is shown to be inactive. The child with a fresh primary complex should also be kept under separate supervision. The whole group should be given special consideration as to rest and fresh air.

LESLIE, Evanston, Ill.

RESULTS OF THE BATTLE AGAINST CHILDHOOD TUBERCULOSIS ORGANIZED UNDER MEDICAL SUPERVISION. M. COFFIN, Paris méd. **1**:26 (Jan. 2) 1937.

This article shows the excellent results which may be obtained when there is close cooperation between those supervising adults with tuberculosis and those whose interest is chiefly in the tuberculosis of childhood.

LESLIE, Evanston, Ill.

A CASE OF SYPHILIS WITH ASYMPTOMATIC FEVER AND AN UNUSUAL COURSE. M. ORTOLANI, Lattante **8**:59 (Feb.) 1937.

A boy aged 9 had as the only sign of illness a fever which after a month was finally ascribed to syphilitic infection. Following treatment with neoarsphenamine

and mercurial inunctions, he began to have arthritis, involving especially the knee joints; the fever persisted. One month later, as these symptoms began to subside there appeared acute interstitial keratitis and papular syphilids; these lasted for a month. Fifteen days later there were marked edema and nephrosis, characterized by the presence of 2.5 Gm. of albumin per liter in the urine. The nephrosis persisted until specific treatment was discontinued.

HIGGINS, Boston.

NEW OBSERVATIONS ON SYMPTOMS OF CATALEPSY IN TUBERCULOUS CHILDREN. P. LUCIANI, Lattante **8**:68 (Feb.) 1937.

Two cases are reported, one of a child of 17 months, and the other of a child of 4½ years, both of whom subsequently died of extensive pulmonary tuberculosis. Both of these children demonstrated cataleptic phenomena during the last months of their lives.

HIGGINS, Boston.

A DEMOGRAPHIC STUDY OF CONGENITAL SYPHILIS IN ITALY. F. LISI, Lattante **8**:75 (Feb.) 1937.

Lisi has assembled a vast amount of data from various clinics, from literature and from government records regarding the extent of syphilis in Italy. Complete data admittedly cannot be obtained regarding social diseases, and comparisons with other countries are not reliable.

*Fecundity of Syphilitics.*—Although statistics are somewhat contradictory, the weight of evidence seems to point toward a deleterious action of syphilitic infections, both acquired and congenital, on fecundity.

*Abortions and Syphilis.*—Of from 70,000 to 100,000 abortions each year in Italy, approximately 10 per cent are due to syphilis.

*Syphilis and Stillbirths, Neonatal Mortality and Prematurity.*—In Italy, syphilis is estimated to be responsible for between 5 and 10 per cent of the total number of stillbirths. The stillbirths in 1935 totaled 33,849, or 32.8 per thousand births; between 2,000 and 4,000 were due to syphilis. In 1935 there were 125 deaths from syphilis during the first six days of life. Approximately 15 per cent of stillbirths and neonatal deaths were of illegitimate offspring. About 20 per cent of the stillbirths were premature, the other 80 per cent occurring at term. Statistics from various clinics in Italy show that premature parturition in syphilis occurs in between 5 and 50 per cent of syphilitic mothers.

*Syphilitic Infantile Mortality and Morbidity.*—In 1934 the mortality from syphilis in infants who were in the first year of life was 4.3 per thousand live legitimately born babies and 41 per ten thousand live illegitimately born babies. Of 1,563 yearly deaths from syphilis, 611 were of babies who were in the first year of life and 29 of children who were between 1 and 4 years of age.

In conclusion, Lisi advocates the dissemination to the public of information on the damage done by syphilis, on the efficacy of treatment and on the need of examinations before marriage and at the beginning of pregnancy. He urges suitable gratuitous treatment for pregnant women and infants with syphilis and the institution of consultation service in every city in Italy.

HIGGINS, Boston.

MEINICKE'S REACTION. A. SELLEK AZZI and A. DEL FRADE, Arch. de med. inf. **6**:108 (March) 1937.

This is the final article on Meinicke's test. Several have been abstracted from this journal. Seven of 100 normal persons had this reaction as well as the Kahn reaction positive. In every case of a positive reaction syphilis was found. Among 351 persons sick from causes other than syphilis, there were a few with positive reactions. Again these were found to be syphilitic. Among 10 persons with malaria there was only one positive reaction, and this occurred in the case of a person who was shown to be syphilitic.

SANFORD, Chicago.

CONGENITAL SYPHILIS IN THE SECOND AND THIRD PERIODS OF CHILDHOOD. A. CARRAU, Bol. Inst. internac. am. de protec. a la infancia **10**:386 (Jan.) 1937.

At the present moment, some points should be set forth: In the first place is that of the attenuation of the disease. This attenuation has been verified in France, Germany and other lands and has been pointed out by Torres Umaña in Colombia, by Navarro in Argentina and by Lorenzo y deal and Etchelar in Uruguay. It is partially due to the effective action of the medicine employed, also, indirectly, to the better and earlier recognition of the disease, for the early diagnosis has allowed early treatment. The attenuation of the disease is evidenced in clinical forms with few and weak symptoms. Recognition of the disease is made difficult in many such cases.

Together with the attenuation, one should know the particular chronological distribution of the disease in relation to the sick child's age. In the first year the symptoms are varied. On passing to the second and third years, there is a period of quietness, interrupted at times by cutaneous lesions. The diseases of the second and third years are hematosyphilis (splenic anemia and pseudoleukemia) or neurosyphilis (convulsions, hemiplegia and like manifestations). After the fourth year there is a new phase, characterized by the dispersion of the clinical aspects. One should recall the following lesions: of the teeth, Hutchinson's teeth, of the incisive germ; of the eyes, keratitis; of the ear, deafness; of the articulations, hydarthrosis; of the viscera; hepatopathy, splenopathy, pneumopathy, etc. After childhood, in adolescence, specific manifestations, such as tabes and dementia paralytica, may occur, though not frequently.

In the third place, it is well to point out that there is an extraordinary variety and multiplicity of clinical symptoms in the second and third periods of childhood. Together with syphilis diagnosed clinically there exist syphilis diagnosed serologically and roentgenologically. The diagnosis of late syphilis is often dependent on not only minute clinical examination but also complete study of antecedents and serologic roentgenologic observations. FROM THE AUTHOR'S SUMMARY.

THE SERODIAGNOSTIC TEST OF MEINICKE IN TUBERCULOSIS, ESPECIALLY IN CHILDHOOD TUBERCULOSIS. G. MELODIA, Med. inf. **8**:37 (Feb.) 1937.

Meinicke in 1934 described a new serum reaction for the diagnosis of tuberculosis, using antigens of his own preparation (*Klin. Wchnschr.* **13**:833, 1934). With this test Melodia has made observations on the blood serums of ninety patients (nine adults and eighty-one children). Sixty were affected with tuberculosis, twenty had other diseases, and ten were healthy.

In only one of nineteen patients with pulmonary tuberculosis was the test negative. Of twelve with tracheobronchial tuberculous adenitis, ten had a positive and one a doubtful reaction. In one the test was negative. Of twenty-four with tuberculous osteo-arthritis, twenty-two had a positive and two a doubtful reaction. Those who gave a doubtful or no reaction had had the disease for only a short time or were very sick or dying.

In all the patients with other diseases the tuberculin test was negative, and in ten the Meinicke test was negative; one showed a faintly positive Meinicke reaction (chronic articular rheumatism) and one a doubtful reaction (pertussis). In healthy persons the test was always negative.

Melodia concludes that the test of Meinicke is usually specific for tuberculosis and that it is as adaptable to tuberculous children as to tuberculous adults.

HIGGINS, Boston.

MATHEMATICAL STUDY OF THE DECLINE OF PULMONARY TUBERCULOSIS IN CIVILIZED NATIONS. M. EICHINGER, Arch. f. Hyg. **117**:245 (Feb.) 1937.

The mortality statistics of pulmonary tuberculosis in various civilized nations are subjected to detailed mathematical analysis. The decline is strikingly illustrated by numerous graphs and tables.

GLASER, Rochester, N. Y.

PIRQUET REACTION IN RELATION TO DIFFERENT MANIFESTATIONS OF TUBERCULOSIS. P. KASSAY-FARKAS, Arch. f. Kinderh. **110**:31, 1937.

The tuberculin reaction was observed as to its beginning, clinical appearance, duration and course in 100 children. On the whole the reaction showed little variation, but the following exceptions were seen: In erythema nodosum the reaction appeared very early, was usually very strong and disappeared quickly. The reverse was observed in scrofula; i. e., slow development, the reaction reaching its height only after two days, and long duration, up to fourteen days.

Five children under 1 year of age in whom no signs of a tuberculin infection could be discovered then or later showed a positive reaction. This is considered a pseudoreaction.

CRANE, Washington, D.C.

BRONCHOPNEUMONIA-TUBERCULOUS INFILTRATION OF THE LUNG. H. OPITZ, Kinderärztl. Praxis **8**:64 (Feb.) 1937.

A report is given of three cases in which differentiation between bronchopneumonia and pulmonary tuberculosis in young children proved to be very difficult. In favor of a diagnosis of tuberculosis may be findings otherwise characteristic of pneumonia associated with fever lasting for over two to three weeks. The possibility of tuberculosis is especially likely if the child is in good general condition. Physical findings may be minimal as compared with those in roentgenograms. Epituberculous infiltrations frequently are localized in the upper lobes; dulness is often marked, while auscultatory signs are comparatively rather meager. Moderate leukocytosis and only slight increase in the sedimentation rate of red blood cells also speak in favor of epituberculous infiltration. Any case of so-called pneumonia in which some of these conditions are present warrants an intracutaneous tuberculin test.

HEYMANN, Cleveland.

EXPERIENCES WITH A DERIVATIVE OF SULFANILAMIDE, PRONTOSIL SOLUBLE (THE DISODIUM SALT OF 4'-SULFAMIDOPHENYL-2-AZO-7-ACETYLAMINO-1-HYDROXYNAPHTHYLENE-3, 6-DISULFONIC ACID) IN THE TREATMENT OF INFECTIONS OF THE URINARY TRACT. W. MEISSNER, Med. Klin. **33**:95 (Jan. 15) 1937.

The fact that this dye (about which much has been written during the past two years) is excreted via the urinary tract and imparts a yellowish red color to the urine gave rise to the idea that it might be effective in the treatment of pyelocystitis. Seven of eight adults (seven women and one man) who were treated with it recovered in from seven to ten days. One had a mild recurrence. The single patient showing incomplete recovery was apparently observed only four days. Most of the patients had Bacillus coli infections of the urinary tract.

SIEMSEN, Chicago.

ROENTGEN FEATURES OF OSSEOUS TUBERCULOSIS: CYSTIC TUBERCULOSIS OF THE ILIUM. F. WINDHOLZ, Röntgenpraxis **9**:41 (Jan.) 1937.

According to Rebaudi, in only 1.8 per cent of cases of tuberculosis of the skeleton do lesions occur in the pelvis; in less than a tenth of such cases is the infection localized in the ilium. Windholz reports the case of a 14 year old boy who had complained of discomfort in his right hip for a period of eighteen months. Roentgenographic examination showed a large number of cystic lesions in the right ilium. Aspiration of one of the cysts yielded a viscid yellow fluid, which contained granular purulent material. Although acid-fast organisms were not demonstrated either by direct smear of the fluid or by inoc
the tuberculin test was positive. There was roentgen evide ce o
tuberculosis of the lungs.

A second case is reported in which a patient who was suffering from tuberculosis of the hip also showed roentgen evidence suggestive of extension of the process to the ilium.

MCCUNE, New York.

ATYPICAL LOCALIZATION OF OSTEITIS TUBERCULOSA MULTIPLEX CYSTICA. E. HERSKOVITS, Röntgenpraxis **9**:45 (Jan.) 1937.

Herskovits reports a case of multiple cystic tuberculosis of bone. The lesions were located in the mandible, os pubis and proximal third of each femur. These sites are atypical, but the diagnosis of tuberculosis was rendered plausible by the later occurrence of hematogenous involvement of the lungs.

McCUNE, New York.

TUBERCULOSIS OF THE OS PUBIS. BERGERHOFF, Röntgenpraxis **9**:130 (Feb.) 1937.

This is a report of the case of a 5 year old girl with myelitis of the os pubis which was thought to be due to tuberculosis. Although the diagnosis was not verified histologically or bacteriologically, it received confirmation from the fact that a short time after roentgen examination the child died of tuberculous meningitis.

McCUNE, New York.

SYPHILITIC PEMPHIGUS BEGINNING ON THE DORSAL REGIONS OF THE HANDS AND FEET. A. IANCU and I. VOICU, Spitalul **56**:436 (Nov.) 1936.

This is a report of a case of syphilitic pemphigus in a new-born infant of 4 days. The first lesions were localized in the dorsal regions of the hands and feet and were in the nature of papulobullous syphilids.

AUTHORS' SUMMARY.

VERIFICATION OF TUBERCLE BACILLI IN THE BLOOD STREAM. K. FUKUMOTO, J. Orient. Med. **26**:261 (Feb.) 1937.

Fukumoto employed the methods of culture devised by Löwenstein and by Iibuchi modified by the addition of 5 per cent sulfuric acid. When 1 mg. of bacilli was injected, the organism continued to be present in the blood stream for seven days, and with 3 mg., for more than fourteen days. Blood cultures from the tuberculous animals which had received 0.05 cc. of tuberculin were consistently negative.

KATO, Chicago.

## Diseases of Blood, Heart and Blood Vessels, and Spleen

HEART DISEASE IN CHILDREN: CERTAIN ASPECTS OF THE AGE AT ONSET AND OF RECURRENCES IN FOUR HUNDRED AND EIGHTY-EIGHT CASES OF JUVENILE RHEUMATISM USHERED IN BY MAJOR CLINICAL MANIFESTATIONS. I. R. ROTH, C. LINGG and A. WHITTEMORE, Am. Heart J. **13**:36 (Jan.) 1937.

In a study of 488 cases of juvenile rheumatism, it was found that the mean age at onset was 8 years, and the mode, 7 years. The mode varied with the clinical type of the initial illness, being about 5 years in polyarthritis, 6 years in carditis and between 7 and 8 years in chorea.

The average duration of the period of observation was eight years. During this period at least one recurrence took place in 68 per cent. In most instances there were only one or two recurrences, but in an appreciable number three or more recurrences were observed.

The first recurrence appeared not later than three years after the initial manifestation of the disease in 73 per cent. The type of the recurrences was usually the same as that of the initial attack.

GIBSON, Chicago.

ESTIMATION OF CARDIAC FUNCTION BY SIMPLE CLINICAL METHODS. E. MESSINGER, Ann. Int. Med. **10**:986 (Jan.) 1937.

The article deals with the determination of the functional impairment and of the cardiac reserve of ambulatory cardiac patients free from the influence of drug therapy. The criteria selected for this appraisal were tachypnea and the ratio of pulse rate to respiratory rate after exercise.

READING, Galveston, Texas.

THROMBOPENIC PURPURA ASSOCIATED WITH CATARRHAL JAUNDICE: REPORT OF A CASE. H. L. ALT and R. L. SWANK, Ann. Int. Med. **10**:1049 (Jan.) 1937.

The patient was a medical student aged 24. Thrombopenic purpura occurred simultaneously with an attack of acute catarrhal jaundice. The authors suggest that there is a relationship between thrombopenia and disease of the liver. Various theories in support of this relationship are given.

READING, Galveston, Texas.

CHLOROMA: REPORT OF A CASE. H. R. ROEHM, A. RIKER and R. E. OLSEN, Ann. Int. Med. **10**:1054 (Jan.) 1937.

The case is that of a girl aged 13 years. Accompanying the report is the protocol of a complete necropsy. The illustrations are excellent.

The term "chloroma" is considered a faulty designation, as the green coloration is not specific for any one type of tumor cell. The green pigment is due to phagocytosis of blood in obstructed capillaries by the endothelial cells.

READING, Galveston, Texas.

VARIOUS ACTIVITIES OF THE BEATING HEART. E. KEATING, Illinois M. J. **71**:63 (Jan.) 1937.

In this discussion of the mechanics of normal and of damaged hearts Keating emphasizes the importance of chronic mild infections in childhood in heart disease, the importance to the damaged heart of prolonged rest, and the use and abuse of digitalis.

BARBOUR, Peoria.

THROMBOCYTOPENIC PURPURA DUE TO FOOD ALLERGY. T. L. SQUIER and F. W. MADISON, J. Allergy **8**:143 (Jan.) 1937.

The authors regard food allergy as one of the causes of essential thrombocytopenic purpura. They report several cases in which definite improvement was shown when foods which gave positive reactions were eliminated from the diet. The thrombocytes and leukocytes, which were markedly decreased, and the eosinophils, which were increased, in number, returned to normal, as did the bleeding time and the clot retractility. Each test was done on a fasting stomach in the morning. Thrombocyte, leukocyte and eosinophil counts were done at three minute intervals before ingestion of a test food, and at fifteen, thirty, sixty and ninety minute intervals subsequent to ingestion.

One patient improved when potato was eliminated from the diet; another, when milk and potato were eliminated, and another when wheat was eliminated.

It is believed that anaphylactoid purpura and thrombocytopenic purpura are the result of an allergic reaction; in the former this reaction is manifested by increased permeability of capillary walls, and in the latter, by a reduction in the number of thrombocytes with an associated effect on the bleeding time and clot retractility.

HOYER, Cincinnati.

THE SIGNIFICANCE OF, AND A DIFFERENTIAL DIAGNOSTIC TEST OF, PRECORDIAL MURMURS IN CHILDREN. M. M. MALINER and I. OKIN, J. Pediat. **10**:77 (Jan.) 1937.

Maliner and Okin, believing that frequently heart murmurs that are classed as functional are found, after a period of observation, to be of organic origin, devised a means of accentuating and localizing these murmurs by the use of a subcutaneous injection of epinephrine in 1:1,000 dilution. Five years ago thirty-two children with a clinical diagnosis of functional cardiac disturbance were given the epinephrine test. Following the test the condition in twenty-three of these was diagnosed as organic valvular heart disease. Reexamination after five years showed that eleven of these twenty-three children, or 47.8 per cent, suffered from definite valvular defects. The test appeared to be 100 per cent correct for children over 10 years of age, but of less value for children under this age.

The test was repeated on thirty-seven children who were clinically in class "E" according to the criteria of the New York Heart Association. Twelve of these children were given a preliminary test with amyl nitrite. There was no uniformity in the results of the two tests, and the authors believe that the amyl nitrite test for accentuating organic cardiac murmurs is unreliable. In twenty-three of the thirty-seven children the intensity of the murmur was definitely increased following the injection of epinephrine, and the authors feel that these twenty-three children, or 62.1 per cent of the group, are in all probability suffering from organic heart disease in an early phase. Because of these results the authors urge the physician to be cognizant of the threatening importance of the cardiac murmur, even without the expectant concomitant signs or symptoms of organic valvular heart disease.

RAUH, Cincinnati.

DIAGNOSIS OF LEUKEMIA IN CHILDHOOD. A. ABT, M. Clin. North America **21**:89 (Jan.) 1937.

The diagnosis of leukemia in infancy and childhood may offer no particular difficulty in cases presenting classic symptoms and running a typical course. However, the many variations from the norm and the close simulation of this disease by other conditions is strikingly shown by Abt in a series of case histories, which make up the bulk of his paper. He illustrates his points by grouping his cases under the following headings:

(A) Nonleukemic conditions simulating leukemia: Group I. Differentiation when leukocytosis is present.

1. Pertussis
2. Pneumonia
3. Sepsis
4. Von Jaksch's pseudoleukemic anemia
5. Cooley's Mediterranean erythroblastic anemia
6. Infectious mononucleosis
7. Mediastinal tumor
8. Essential lipoid histiocytosis of Niemann and Pick

(B) Leukemia simulating other conditions:

1. Simulating mediastinal tumor
2. Simulating rheumatism
3. Simulating diarrhea
4. Simulating parotitis

(A) Nonleukemic conditions simulating leukemia: Group II. Differentiation when leukopenia is present.

1. Sepsis
2. Agranulocytosis
3. Gaucher's disease
4. Nonlipoid splenohepatomegaly; Letterer-Siwe disease
5. Malaria

(B) Aleukemic leukemia simulating other conditions:

1. Simulating sepsis
2. Simulating appendicitis
3. Simulating aplastic anemia

From the differential diagnostic point of view this is a most instructive group of case histories. The original paper should be consulted by those who are puzzled by the vagaries of the hematology of childhood.

EUGENE SMITH, Ogden, Utah.

DIAGNOSIS AND TREATMENT OF ANEMIA: VIII. ANEMIAS OF INFANCY. J. C. SHARPE, Nebraska M. J. **22**:16 (Jan.) 1937.

While at birth it is not unusual to find a hemoglobin content of 120 per cent and erythrocytes numbering from 6,000,000 to 7,000,000 per cubic millimeter, a rapid decline in the hemoglobin and red blood cells occurs in all infants during the first eight to ten weeks. A normal infant possesses five times as much iron per gram of body weight as does an adult. Demands on the blood-forming organs during the first year, owing to the rapid growth, are heavy. About the fourth month the infant's reserve of hemoglobin is depleted, and formation of blood must wait the addition of iron from the mixed diet. The prophylactic administering of iron to infants during the first two months does not prevent or alter the occurrence of the aforementioned apparently physiologic anemia. Most clinicians agree that the anemia of the premature infant cannot be prevented wholly by intramuscular injections of human blood or by administration of copper and iron or of liver extract. Later iron is more efficient. So-called nutritional anemia of the infant is usually due to a deficiency of iron; either the iron reserve is inadequate or the supply in the infant's diet is insufficient. Both breast milk and cow's milk are low in iron, and the mixed diet containing iron may be too long postponed. Infection is the most common etiologic factor. Anemia usually results from sepsis. The removal of the focus of infection is of prime importance. In severe anemia, transfusions may be necessary.

HAMILTON, Omaha.

CONGENITAL ABSENCE OF THE PERICARDIUM WITH REPORT OF A CASE. W. E. LADD, New England J. Med. **214**:183 (Jan. 30) 1936.

The patient was born at full term and by normal delivery. The birth weight was 7 pounds and 14 ounces (3,572 Gm.). When feeding was attempted, the baby became cyanotic, choked and regurgitated. This difficulty appeared to be more marked with breast than with artificial feeding. At this time diaphragmatic hernia was suspected and confirmed by roentgen studies. From that time until she was 2 years old and entered the Children's Hospital, Boston, she had measles, German measles and chickenpox. She weighed 18 pounds (8,164.6 Gm.).

At operation, above the opening in the diaphragm, in the thoracic cavity were found the stomach, spleen and splenic flexure, half the transverse colon and about 4 or 5 inches (10 or 12 cm.) of the descending colon. These organs were very easily delivered from the thoracic cavity. On looking through the opening in the diaphragm the lung was seen collapsed, and the heart next to it, in the same cavity without any pericardial covering. The hernial opening in the diaphragm was closed.

The first twenty-four hours after operation were somewhat stormy, but convalescence progressed satisfactorily and uninterruptedly. A follow-up examination was made four months after operation. The child had gained 4 pounds (1,814 Gm.) in weight, had a good appetite and normal movements of the bowels. The roentgen examination showed the diaphragm in normal position at the left and moving with respiration. It also showed the stomach and abdominal viscera in normal position.

It is believed that this is the only case of this condition to be recognized during life, but from the literature one may conclude that the condition is compatible with an active life of normal duration.

GENGENBACH, Denver.

REVERSION OF CARDIAC ENLARGEMENT IN A FOUR YEAR OLD CHILD FOLLOWING TREATMENT FOR AVITAMINOSIS. L. RABINOWITZ and E. J. ROGERS, New England J. Med. **215**:621 (Oct. 1) 1936.

The case presented is that of a 4 year old boy with chronic avitaminosis and cardiac enlargement, which disappeared following adequate treatment for the avitaminosis. At about 10 months of age he suddenly began screaming when his limbs were handled. The family called a chiropractor who gave the child "adjustments." These "worked." The "large black circles" under the child's eyes disappeared.

The child was late in sitting and standing. He did not begin to walk until about three years and nine months after birth. He never ate well, and it was not until then that he had any solid food, which consisted of some bread, jelly and cake—the only other food or medicament being milk and "Karo syrup." The child had had measles, chickenpox and whooping cough. Physical examination disclosed a 4 year old white male child, 30 inches (76 cm.) long and weighing 27 pounds (12 Kg.). Small orbital hemorrhages were present. The gums were deep bluish purple, and those about the upper central incisors were spongy. They bled easily with some slough of tissue.

Loud blowing systolic and diastolic murmurs were heard over the mitral area, transmitted to the axilla and back and entirely obliterating the heart sounds. Pain and tenderness were noted in all joints, increasing on motion.

Examination of the blood disclosed hemoglobin 25 per cent, red blood cells 1,950,000 and white blood cells 5,500. The coagulation time was increased. The red cells showed extreme achromia, anisocytosis and poikilocytosis. The urine was essentially negative except for a high concentration of urates.

Roentgen examination of the chest showed marked enlargement of the cardiac shadow. The child was put to bed, and a varied diet was offered him, high in vitamin C and accompanied by liver concentrate, iron and viosterol. About three weeks after entry the hemoglobin rose to 55 per cent, and the red blood cell to 3,250,000. Five months later, the hemoglobin was 90 per cent and the red blood cell count 4,900,000. The x-ray picture of the chest at this time showed recession of the cardiac shadow to within normal limits.

GENGENBACH, Denver.

ABSENCE OF EFFECT OF SWALLOWED SALIVA ON COAGULATION OF BLOOD. H. D. FAYLE and F. H. SCOTT, Proc. Soc. Exper. Biol. & Med. **35**:594 (Jan.) 1937.

It has been shown that saliva added to shed blood has a remarkable clot-accelerating action, whether the blood is normal or hemophilic. Swallowing of excessive amounts of saliva and extirpation of the salivary glands have no effect on the coagulation time of the blood.

HANSEN, Minneapolis.

NUTRITIONAL ANEMIA IN THE EAST END OF LONDON. L. FINDLAY, Brit. M. J. **1**:12 (Jan. 2) 1937.

A study was made of 290 patients admitted during two years to the Princess Elizabeth of York Hospital for Children, in an effort to ascertain, if possible, whether nutritional anemia is common in the poorer walks of life in London in this particular area. The conclusions of the study are summed up as follows: Examination of the blood of sick children in the East End of London reveals for the most part that the values for hemoglobin and red cells are normal. Anemia when present during infancy is most frequent during the first three months and is probably the result of congenital causes or of hemorrhage at birth. Anemia occurring during later infancy and childhood is rare and when present is probably the result of a toxic condition. There is no evidence from the section of the population studied that nutritional anemia is common.

ROYSTER, University, Va.

INFLUENCE OF EXTERNAL TEMPERATURE ON THE BLOOD SEDIMENTATION RATE. D. B. ROSENTHAL, M. J. Australia **1**:172 (Jan. 30) 1937.

By simple experiment Rosenthal shows that there is a definite relationship between the sedimentation rate and the external temperature. The higher the temperature the more rapid is the sedimentation rate, and the change in rate is roughly proportional to the change in temperature. For example, a sedimentation index of 17 mm. on a summer day may well be the equivalent of 5 mm. in the same specimen on a winter morning; a "diagonal curve" on a hot day might have the same significance as a "horizontal line" during a cold spell. This alteration

of rate is attributed mainly to the change in viscosity of the blood plasma. Mathematical correction for variation in temperature is at present impracticable and therefore a complete statement of the result of a sedimentation test should include the room temperature as well as the hematocrit value. GONCE, Madison, Wis.

SYNDROME OF GLANZMANN'S ESSENTIAL THROMBO-ASTHENIA IN THE CHILD. E. H. CONITZER, Riv. di clin. pediat. **35**:41 (Jan.) 1937.

Conitzer reviews the cases of hereditary thrombo-asthenic purpura presented by Glanzmann and maintains that the hereditary factor does not follow the law of Mendel. It is noted that the transmission is usually through the female, but that both male and female may be involved. In evaluating thrombo-asthenia the retractility of the clot and the nature of the platelets themselves are considered. In Glanzmann's disease the number of platelets is usually not diminished, although the retractility of the clot may not be normal; this indicates that the platelets are not normal in function or in anatomy.

The conclusion is drawn that Werlhof's purpura haemorrhagica and Glanzmann's hereditary thrombo-asthenic purpura are separate diseases.

HIGGINS, Boston.

CONSTITUTIONAL HEMOLYTIC JAUNDICE. F. SEMAH, Riv. di clin. pediat. **35**:97 (Feb.) 1937.

This is a review of clinical, etiologic and biochemical facts relating to hemolytic jaundice in children. An extensive bibliography accompanies the article.

HIGGINS, Boston.

A CASE OF DIFFUSE DILATATION OF THE PULMONARY ARTERY DUE TO CONGENITAL INSUFFICIENCY OF THE PULMONARY VALVE. A. KAUTZKY, Röntgenpraxis **8**:809 (Dec.) 1936.

The lesion, which presumably was present at birth, persisted throughout life. The diagnosis was made roentgenographically when the patient was 62 years of age and confirmed at autopsy. The differential features are discussed.

MCCUNE, New York.

PRACTICAL IMPORTANCE OF THE SEDIMENTATION RATE. H. REICHEL, Wien. klin. Wchnschr. **49**:1517 (Dec. 11) 1936.

Reichel reports that the sedimentation rate may be useful in clinical diagnosis of many diseases. In infections without local inflammation, the sedimentation is normal; when local inflammation occurs, the sedimentation occurs more rapidly. For example, in uncomplicated influenza, even with high fever, the sedimentation is accelerated, and hence the sedimentation test can be used to diagnose this complication before chemical signs appear.

In tracheitis and bronchitis the sedimentation rate is normal. In pneumonia, abscess, gangrene and pleurisy there is marked increase in the rate, and the more serious the inflammation or the necrosis the faster do the erythrocytes sink.

Diseases of the circulatory organs, even when decompensation occurs, do not cause changes in sedimentation. However, local inflammations, such as myocarditis, bring about rapid sedimentation. Syphilitic mesaortitis usually is accompanied by rapid sedimentation.

The extent of the necrosis in the heart muscle in coronary thrombosis can be judged very exactly after twenty-four hours of resorption; the more rapid the rate, the more serious is the condition.

The sedimentation test is a means of distinguishing between types of icterus. Normal sedimentation occurs in nine tenths of the uncomplicated cases of parenchymal icterus, icterus catarrhalis and arsphenamine icterus. Rapid sedimentation is a sign of a more serious type: infectious icterus (Weil), icterus due to cirrhosis of the liver, epidemic icterus in children and other forms.

Sedimentation is a guide likewise in diagnosis of diseases of the joints, bones and nerves. In polyarthritic rheumatism in the acute stage, sedimentation is extraordinarily rapid, more so than in any other disease (owing, no doubt, to the extent of the infection). On the other hand, sedimentation is normal in cases of degenerative (but not serous) joint diseases, such as arthropathia deformans, tabetica or alkaptonurica.

In the new-born infant rapid sedimentation is a sign of active congenital syphilis. The test is also useful in confirming the suspicion of tuberculosis in children, especially as a complication of measles or pertussis; when the complication is present, an increase in the sedimentation rate occurs.

Repeated tests chart the course of the illness and are especially advisable in acute nephritis, acute pyelitis, acute polyarthritis, pernicious anemia and other serious conditions in which prognosis is otherwise uncertain.

Finally, the test has a bearing on therapy. While there is rapid sedimentation in joint diseases, salicylate treatment should be continued (provided the temperature and the blood picture otherwise remain normal).

Whenever sedimentation is accelerated, irritating therapy is contraindicated. The explanation of the phenomenon depends on the physical law that the rapidity of sedimentation of round bodies in a liquid is quadratically proportional to the radius of the sinking bodies. Erythrocytes in the blood sink not as units but *en masse*. The agglomeration of the erythrocytes is affected by the fibrinogen and globulin of the blood, which in turn are affected by various diseases. If the agglomeration is encouraged so that the erythrocytes accumulate in large masses, they sink proportionately more rapidly.

ABT, Chicago.

PAROXYSMAL TACHYCARDIA IN A CHILD OF THREE YEARS. F. S. P. VAN BUCHEM and J. L. KEYZER, Nederl. tijdschr. v. geneesk. **80**:5005 (Nov. 7) 1936.

After a review of the cases of paroxysmal tachycardia in children described in recent years the authors give a detailed record of a case observed in a child, aged 3, with the cardiographic findings which demonstrated an auricular paroxysmal tachycardia. By comparison and analysis of the graphs taken successively, the existence of a parasystole could be proved, and the incidence of the paroxysms of tachycardia was in accordance with a scheme recently published by Lohr (dissert., Amsterdam, 1936). During the attacks the authors were not able to observe any abnormalities of the blood sugar, nor could they obtain any improvement of the tachycardia by giving sugar.

VAN CREVELD, Amsterdam, Netherlands.

PORPHYRIN IN NORMAL BLOOD CELLS. W. GROTEPASS, Nederl. tijdschr. v. geneesk. **81**:362 (Jan. 23) 1937.

Grotepass, working in the clinic of Hymans van den Bergh, gives a review of the main data from porphyrin research. He shows that the protoporphyrin in normal human corpuscles is derived from aetioporphyrin III.

VAN CREVELD, Amsterdam, Netherlands.

## Diseases of Nose, Throat and Ear

THE STAPHYLOCOCCUS IN RELATION TO SINUSITIS, BRONCHITIS AND BRONCHIECTASIS. FLETCHER D. WOODWARD, Arch. Otolaryng. **24**:753 (Dec.) 1936.

The author reports the high frequency of hemolytic and nonhemolytic staphylococci in cultures of material taken from the spheno-ethmoid region. The method of taking material for these cultures is given, and the statement is made that the report is based entirely on a summary of clinical impressions.

The bacteriology of the staphylococcus is reviewed. Treatment with antitoxin and toxoids is discussed relative to cases of acute and chronic sinusitis and of chronic sinusitis complicated by chronic bronchitis and bronchiectasis. Although labora-

tory research and clinical observations are too recent to warrant positive statements, future work along these lines will undoubtedly prove the definite value of this therapy in conjunction with the older, well known methods of treatment.

GREENWOOD, Chicago.

USE OF BENZEDRINE VAPOR IN CHILDREN. J. A. SCARANO and J. F. COPPOLINO, Arch. Pediat. **54**:97 (Feb.) 1937.

Benzedrine vapor was used in the treatment of rhinologic infections in 100 children. Prompt and adequate shrinkage of the nasal mucosa occurred, with no secondary reactions, local or systemic.

ORR, Buffalo.

ALLERGY OF THE EYE, EAR, NOSE and THROAT. L. UNGER, Illinois M. J. **71**:47 (Jan.) 1937.

Unger points out that one who has allergic symptoms in any part of his body is apt also to have evidence of hypersensitivity in another organ. There is usually an increase in the percentage of eosinophils in the blood and also in the secretions of the eyes, nose and bronchial tubes. Hay fever from pollen is probably the most frequent cause of allergy in the eyes. Vernal conjunctivitis has not been definitely proved to be allergic. The results of treatment from the allergic point of view have not been very satisfactory. So-called nonseasonal allergic conjunctivitis is due to sensitization to some substance other than pollen. In treatment, the specific cause should be removed as far as possible. When complete removal of the cause cannot be carried out, desensitization should be attempted. Patients with contact dermatitis of the eye are not allergic in the ordinary sense of the term. They do, however, usually react positively to the patch test. Recent work indicates that allergy is an important, perhaps the sole, cause of Ménière's syndrome. Because of the serious nature of the condition, all patients with Ménière's disease should be subjected to a complete examination, including test for allergy. A large percentage of patients seen in the practice of a rhinologist are definitely allergic. Routine examinations of nasal secretions will change old methods of treatment. Patients with mucous polypi are definitely allergic. The best treatment to date for hay fever from pollen remains the injection of the appropriate extract of the pollen. The value of nasal ionization is still in dispute; its results in hay fever from pollen usually are not good; in the treatment of vasomotor rhinitis some workers report considerable success.

BARBOUR, Peoria.

EXPERIMENTAL VACCINATION AGAINST COLDS IN AN INFANTS' HOME. M. J. WALLFIELD, J. Pediat. **10**: 69 (Jan.) 1937.

Children in the Infants' Home, Brooklyn, who had had frequent colds and involvement of the upper air passages were chosen for the experiment. The ages ranged from birth to 6 years. In 1933 a commercial catarrhal vaccine (called vaccine B in the paper) was used. The following year, in addition to the commercial vaccine, a nonspecific vaccine (called vaccine A in the paper), obtained from saprophytic bacteria of the air, was used. The injections were begun in October of each year. One course of eight subcutaneous injections was given at the rate of two injections a week. The initial dose was 0.1 cc., and subsequent doses were increased gradually to 1 cc., a total of 4.6 cc. being given to each child. In each experiment the period of observation lasted for one year. All temperatures over 100 F. were recorded, as well as the type and number of infections of the upper respiratory tract. Twenty-four children were given injections in 1933 and forty in 1934. The results of the first year showed a reduction of 52 per cent in the number of days of fever and of almost 29 per cent in the number of colds in the vaccinated group. The results of the second year showed no appreciable difference in the number of days of fever and the number of colds between the group given the

nonspecific vaccine A and the group given vaccine B. The nontreated controls showed an increase of 29 per cent in the days of fever and had almost 21 per cent more colds. Wallfield believes that better results might be obtained by increasing the dosage of the vaccine or by using the particular antigen to which the children are sensitive.

RAUH, Cincinnati.

FOREIGN BODIES IN THE AIR AND FOOD PASSAGES. C. I. JOHNSON and C. F. FERGUSON, New England J. Med. **215**:1054 (Dec. 3) 1936.

These cases, seen and followed during one year at the Children's Hospital, in Boston, offer surprisingly wide diversification and are presented in an interesting and thorough manner, with excellent illustrations of the roentgenologic findings. All the patients made good recoveries. The foreign bodies included coins, buttons, safety pins, peanuts and, in one case, a piece of fibrous plant material. The symptoms before examination had persisted for periods varying from a few hours or a few weeks up to eight months (one case in which an upholstery tack was lodged in the left main bronchus).

GENGENBACH, Denver.

LARYNGEAL SYMPTOMS IN CHILDREN. E. J. PATTERSON, Pennsylvania M. J. **40**:257 (Jan.) 1937.

Anatomic differences in the larynx of the child account for difference in symptoms as compared with those of the adult. These alterations are reviewed. The symptoms of congenital and acquired conditions are listed. The author stresses that inferential diagnosis of laryngeal disease in children is a dangerous procedure. Differential diagnosis by laryngoscopy is indicated in all cases. The larynx is easily examined by the direct method in any child, even a new-born one. Tracheotomy, when indicated, is preferred to intubation.

LOGUE, Williamsport, Pa.

A STUDY OF MASTOID INFECTION IN CHILDREN. M. HINES ROBERTS, South. M. J. **29**:1207 (Dec.) 1936.

Many mastoid infections do not require surgical treatment. Persons with such infections frequently present clinical and roentgenographic evidence practically identical with that for patients who finally come to operation.

Even with destruction and necrosis taking place in the mastoid, as shown by roentgen examination, recovery may occur without operation.

Conservative treatment of all patients is recommended, and the author disproves the old idea that early operation for acute mastoid involvement is essential to avoidance of grave complications.

The time element in evaluating all clinical laboratory data is most important. The postponement of operation for one, two or even several days will not endanger the patient and will in most instances obviate the need for surgical intervention.

It is most important to have close cooperation between otologist, roentgenologist and pediatrician, and there should be careful daily comparison of evidence by these three specialists.

SCHLUTZ, Chicago.

THE PREVENTION OF ACUTE SURGICAL MASTOIDITIS. WELCH ENGLAND, West Virginia M. J. **32**:560 (Dec.) 1936.

A certain percentage of infections of the middle ear will heal spontaneously. A certain percentage will go on to mastoiditis, regardless of any or all conservative methods of treatment. Between these two extremes lie the great majority of problems that confront the otologist.

The author discusses the various causes of mastoiditis and concludes that in about 98 per cent of the cases the condition follows an acute infection of the nose and throat, ascending by way of the eustachian tubes.

Most of these cases fall in the age group from 8 to 16 years. With a temperature ranging from 99 to 105 F., profuse perspiration, draining of the ears, and visible clouding of the mastoids under roentgen examination, there is undoubtedly acute mastoiditis, but just as certainly the patient is septic and should not be operated on. Also, a leukocyte count of about 15,000 associated with a shift to the left of the Schilling differential count still indicates a complicated septic form of infection of the upper part of the respiratory tract. A patient should not be operated on at the time of such manifestations, but operative procedure should be delayed until there is a shift back to a more even range of temperature and a more normal Schilling-Kolmer differential count.

Caution and delay are the watchwords in this article.

SHAWKEY, Charleston, W. Va.

INFECTIONS OF THE UPPER RESPIRATORY TRACT IN CHILDREN. H. M. JAY, M. J. Australia **2**:774 (Dec. 5) 1936.

Concerning infections of the upper part of the respiratory tract in children, Jay observes that: they are more potentially serious than those in adults; some children are hypersusceptible to them and have difficulty in throwing them off; defective nasal breathing and malocclusion of the jaws are predisposing factors; allergic states must not be confused with ordinary "colds"; pneumonia is frequently secondary to infection of the sinuses; an infection of a sinus frequently causes persistent "cold"; the first sign of sinusitis may be orbital swelling; a unilateral nasal discharge should always arouse suspicion of a foreign body in the nose; the free use of meat and fruit juices in the diet as a supplement to milk and carbohydrates raises the immunity to infection; calcium therapy is a useful adjunct in treatment; menthol is not acceptable to the nasal mucous membrane; nasal douches are liable to carry infections to the middle ear, and autogenous vaccines have a great influence in cleaning up these infections.

GONCE, Madison, Wis.

A MODIFICATION OF BRAUN'S TONSILLECTOMY. R. MACHADO, Arch. de med. inf. **6**: 75 (March) 1937.

This procedure is illustrated by ten photographs and should be studied in detail by any one interested. The advantages are that traumatism and hemorrhage are reduced to a minimum. Convalescence is shortened, and pain is absent. It is easily applied to a child, and is the author's choice in 90 per cent of his cases.

SANFORD, Chicago.

## Diseases of Lungs, Pleura and Mediastinum

AGENESIS OF THE LUNG: A REVIEW OF THE LITERATURE AND REPORT OF A CASE. S. HURWITZ and H. B. STEPHENS, Am. J. M. Sc. **193**:81 (Jan.) 1937.

Failure of development of a lung is exceedingly rare. A case is reported and the literature on thirty-four additional authentic cases reviewed. Absence of a lung does not necessarily preclude the person's reaching adult life, as fourteen of the thirty-four patients ranged from 5 to 72 years. The left lung seems more frequently involved.

HENSKE, Omaha.

TWICE A HOST TO A BRONCHIAL FOREIGN BODY. C. P. SCHENCK, Arch. Otolaryng. **25**:81 (Jan.) 1937.

Schenck reports the case of a little girl of 5 years who has experienced the presence of a foreign body in the lungs on two occasions. The first was at the age of 14 months, when a broken hand of a china doll was removed from the right main bronchus. Recovery was uneventful.

The second admission occurred at the age of 5 years, after the child had experienced a severe choking spell while eating an ear of corn. Bronchoscopic examination produced two large and three small pieces of a kernel of corn from the right bronchus. Roentgenograms taken before and after removal, as well as pictures of the objects removed, are reproduced. The author concludes that prompt recovery usually follows skilful removal of the foreign body and that no permanent damage is done. Postoperative physical and roentgen examination of the lungs should be a routine procedure.

GREENWOOD, Chicago.

LUNG ABSCESS IN CHILDREN. F. P. MATHEWS, Arch. Pediat. **54**:1 (Jan.) 1937.

Several different factors are responsible for the increase in the incidence of abscess of the lung during the first decade of life. Removal of children's tonsils and better diagnostic methods such as roentgenographic and bronchoscopic examination are the factors mentioned by the author in a review of twelve cases of nontuberculous pulmonary abscess. The location was as follows: right upper lobe in two, right middle lobe in three, right lower lobe in four, left upper lobe in none and and lower lobe in three.

In five cases the treatment was surgical and in seven medical, with two deaths in the surgically treated group. Bronchoscopy or surgical drainage of the abscess should be reserved for cases in which no progress is apparent after six weeks of medical treatment.

ORR, Buffalo.

SOME NOTES ON THE X-RAY TREATMENT OF ENLARGED INFLAMMATORY TRACHEOBRONCHIAL LYMPH NODES IN INFANTS AND CHILDREN. J. R. CARTY and J. C. RUDE, Arch. Pediat. **54**:26 (Jan.) 1937.

Carty and Rude advise roentgen treatment of infected tracheobronchial nodes in infants and children. Their technic is outlined.

ORR, Buffalo.

EXPERIMENTAL LOBAR PNEUMONIA IN THE RAT: A METHOD FOR THE STUDY OF THERAPY IN THIS DISEASE. W. J. NUNGESTER, J. Bact. **33**:72 (Jan.) 1937.

In previous communications Nungester described a method for producing lobar pneumonia in the white rat. He has studied this disease in some 2,000 rats, employing strains of types I, II and III of the pneumococcus. The conditions met with in these experimental lesions, which closely resembled those seen in lobar pneumonia in man, were definitely different from those encountered in pneumococcic peritonitis or septicemia produced in laboratory animals. Hence it seemed that the use of this method for producing lobar pneumonia in the rat might have certain advantages in studies directed at the problems of treatment of this disease.

Various therapeutic procedures were employed to treat rats in which pneumonia had been induced. These procedures included the use of atropine sulfate, pilocarpine hydrochloride, morphine sulfate, increased oxygen tension and a commercial pneumococcus antiserum. The latter had the most marked effect. The results noted were a lowering of the percentage of mortality and of the incidence of pleurisy, a slight lessening of the effect of the disease on body temperature and a decrease in the bacteremia. These results were obtained with type I and type II infections. Type III infections were not influenced by serum therapy.

STOESSER, Minneapolis.

OIL ASPIRATION PNEUMONIA. G. H. FETTERMAN, J. Lab. & Clin. Med. **22**:619 (March) 1937.

Two cases of oil aspiration pneumonia are discussed. The importance of drops of oil used in the nose and of mineral oil as etiologic factors is discussed.

W. MUNAY Galveston, Texas.

PREVENTION OF POSTOPERATIVE PULMONARY COMPLICATIONS. P. P. VINSON, J. South Carolina M. A. **33:** 5 (Jan.) 1937.

The first consideration is a selected group of patients; that is, care must be taken not to operate on those who have chronic respiratory diseases if possible. The major complication is pulmonary embolism. The removal of teeth or operation on the nose or throat at the same time as an abdominal operation should be prohibited. When the patient is ready to leave the operating room, there should be removal of as much mucus as possible from the tracheobronchial tree. The patient should be turned frequently, as anything which will increase respiratory movements assists in preventing pulmonary complications.

WESTON JR., Columbia, S. C.

LOBAR PNEUMONIA IN CHILDHOOD: A FIVE AND A HALF YEAR CLINICAL SURVEY AT A MUNICIPAL HOSPITAL. S. L. ELLENBERG and A. T. MARTIN, New York State J. Med. **37**:119 (Jan. 15) 1937.

This is a clinical survey of 459 cases of lobar pneumonia with a mortality rate of 4.7 per cent.

AIKMAN, Rochester, N. Y.

OXYGEN THERAPY IN THE TREATMENT OF PNEUMONIA. H. J. MOERSCH, Proc. Staff Meet., Mayo Clin. **12**:33 (Jan. 20) 1937.

Oxygen helps to prevent and eliminate anoxemia and pulmonary edema. In the presence of fever there occurs an increase in metabolism with a corresponding increase in oxygen want. Frequently a characteristic drop in temperature occurs after the institution of oxygen therapy. Oxygen also decreases cardiac effort. Pneumonia caused by a relatively avirulent organism, with a high degree of pulmonary edema, responds most favorably to oxygen therapy. The best guides to oxygen dosage are a diminution in pulse rate and a decrease in the number of organisms.

MILLER, South Bend, Ind.

CARCINOMA OF A BRONCHUS IN A BOY AGED NINETEEN. J. G. HAILWOOD, Brit. M. J. **1**:606 (March 20) 1937.

This case of carcinoma of a bronchus is reported because the patient was only 19 years old. Most cases of this kind occur in persons between the ages of 40 and 70 years. Roentgenograms were taken of the patient, and a section of one of the metastases in the wall of the chest was examined. The patient died six weeks after admission to the hospital. No autopsy was made.

ROYSTER, University, Va.

ATTACKS OF APNEA IN YOUNG INFANTS. G. MARIANI-TOSATTI, Nourrisson **24:** 329 (Nov.) 1936.

Protocols are given of cases illustrating the two types of apnea that may occur in early infancy. The first type is thought to be due to direct failure of the respiratory center in the medulla, and in these cases synchronously with the apnea there is gradual slowing of the heart rate from about 120 to 60.

The second type of apnea is due to indirect involvement of the respiratory center and is explained by disturbances of the circulation resulting from cardiac dysfunction. In this type there occurs very suddenly bradycardia, and the outlook is more ominous.

The differential diagnosis is important from the standpoint of therapy. The cases of apnea due to direct failure of the respiratory center respond well to drugs acting directly on this center, especially lobeline. For the other cases no effective treatment is offered.

MCCLELLAND, Cleveland.

SOME OBSERVATIONS ON EMPYEMA IN CHILDREN. F. PONTIERI and F. TECILAZIC, Pediatria **45**:116 (Feb.) 1937.

The authors have studied seventy patients with pneumococcic empyema secondary to bronchopneumonia, whose ages ranged from infancy to 11 years. Epidemiologic, clinical and anatomicopathologic observations were made. They sound a note of warning in their paper "Extensive costal resection is a dangerous procedure not only in adults but in children, particularly in infants." They stress the value of sodium taurocholate especially in infants. The technic of its administration was described by Dr. Cocchi in 1931. However, they admit that surgical intervention between the ages of 2 and 3 years seems to be the more efficacious and logical solution.

PALMIERI, Brooklyn.

LYMPHOSARCOMA OF THE MEDIASTINUM. A. DE REZENDE, J. de pediat., Rio de Janeiro **4**:16 (Jan.) 1937.

An 8 year old white child began to have attacks of lumbar and abdominal pain, associated with prostration and dyspnea. The author observed one of these attacks and saw that the child was suffering from a respiratory difficulty in which the respiratory muscles and the abdominal muscles contracted almost as in tetany. A roentgenogram showed a large mass in the mediastinum, which on biopsy was found to be a lymphosarcoma. The mass disappeared after six exposures to the roentgen rays, and the child has been in good health since.

SANFORD, Chicago.

THE DIAGNOSIS AND THE DIFFERENTIAL DIAGNOSIS OF ENCROACHING PROCESSES AS REVEALED BY BRONCHOGRAM. A. BEUTEL and F. STRNAD, Fortschr. a. d. Geb. d. Röntgenstrahlen **55**:118 (Feb.) 1937.

This is an extensive and copiously documented discussion of expanding lesions of the lung. The pathologic processes are classified according to whether they are purely expansive or also destructive and further according to their position in the lungs. Numerous separate conditions are considered.

McCUNE, New York.

CHRONIC BRONCHITIS AND BRONCHIECTASIS IN CHILDREN. A. KHALIL ABDEL-KHALIK, J. Egyptian M. A. **20**:32 (Jan.) 1937.

This article represents a postgraduate lecture and is a comprehensive review of the two subjects, giving the pathology and symptomatology of each and the methods of treatment, both medical and surgical. For roentgen visualization the author uses a tracheal injection of iodized poppy-seed oil 40 per cent under chloroform anesthesia. He sometimes uses injections of guaiacol cacodylate in addition to postural drainage, vaccinotherapy and, when indicated, surgical intervention.

MULHERIN, Augusta, Ga.

## Diseases of the Gastro-Intestinal Tract, Liver and Peritoneum

THORACIC STOMACH WITH SHORT ESOPHAGUS AND DIAPHRAGMATIC HERNIA. L. BLOCK, A. M. SERBY and S. SALINGER, Am. J. Digest. Dis. & Nutrition **3**:689 (Nov.) 1936.

Thirty-eight patients were studied. An attempt is made to correlate the symptoms that may lead to a diagnosis of thoracic stomach with short esophagus and diaphragmatic hernia. While this is difficult, the following symptoms are suggestive: (1) increased pain or heart burn on lying down; (2) pain in the chest radiating to the left or down the left arm, and dyspnea, neither one of cardiac origin, and (3) difficulty in swallowing of long duration in a patient on whom traumatic stricture, carcinoma of the esophagus or cardiospasm can be ruled out. The actual diagnosis is always made by roentgen examination.

Of the patients studied, in seven the lesion was a para-esophageal hernia. In nineteen the esophagus was shortened, which caused the thoracic position of the stomach. In twelve patients it was impossible to determine the kind of lesion found. For one patient, the diagnosis was made elsewhere.

It is interesting to note that the majority of the patients in whom esophagoscopy was performed as an aid to diagnosis refused to be subjected to esophagoscopy on their return.

MORRISON, Savannah, Ga.

PERFORATED PEPTIC ULCER IN MECKEL'S DIVERTICULUM. J. E. THOMPSON, Ann. Surg. **105**:44 (Nov.) 1936.

*Incidence.*—In this group of thirty-six perforated ulcers, thirty-one occurred in males. The youngest patient was an infant 15 weeks old, and the oldest was aged 53. Thirty-six per cent of the ulcers occurred in children under the age of 6; only one occurred after the second decade of life.

*Past History.*—Many of the patients gave a previous history of frequent attacks of vague abdominal pain, noticed by the mother since infancy. The most important symptom was passage of fresh blood by rectum. The blood was usually in large dark clots, freely mixed with feces and bright red blood. Patients often complained of cramps associated with nausea and followed by fainting. On regaining consciousness there was an urgent desire to "go to stool," with the passage of bright blood. The bleeding may have occurred years ago or only a few hours before perforation.

*Present Illness.*—Perforation was usually preceded by nausea and vomiting. The pain was first at the umbilicus, then to the right of the midline. The temperature at first was only slightly elevated; the pulse, accelerated. There was no blood in the stool at this time. The onset was not so sudden as in perforated duodenal ulcer.

*Diagnosis.*—The diagnosis in cases of perforated ulcer in Meckel's diverticulum is based on the suddenness of attack and the history of former passage of bright red blood by rectum. A gas bubble beneath the right or the left leaf of the diaphragm, as shown by the roentgenogram, makes the diagnosis certain.

*Treatment.*—Immediate operation is in order. The diverticulum should be amputated at its base and the opening in the small intestine closed.

*Mortality.*—In cases reported up to 1936 the mortality was 31 per cent.

The author reports one case.

BANTIN, Omaha.

THE USE OF THE RAW APPLE DIET AND PECTIN-AGAR MIXTURES IN PEDIATRIC DIARRHEAS. J. S. HUNT, Arch. Pediat. **53**:736 (Nov.) 1936.

Fifteen babies with diarrhea were treated with raw apple pulp. The average age of the patients was 14 months. The average period of the raw apple therapy was two and nine-tenths days; the longest was four days and the shortest one day. One failure occurred. Hunt concludes that in private practice the raw apple therapy is preferable to the use of the pectin-agar mixture because it is more easily and cheaply prepared by the housewife.

ORR, Buffalo.

FOODBORNE OUTBREAKS OF GASTROENTERITIS. Health News **13**:202 (Dec. 21) 1936.

Two instances of food poisoning are reported. One occurred in a small club in eastern New York, where twenty-six people had nausea, vomiting and severe diarrhea after eating creamed potatoes. Bacillus dysenteriae (Sonne) was found in the stools of the three patients examined.

In another instance vomiting, diarrhea and abdominal cramps developed in twelve persons after they ate boiled ham. No organisms of importance were detected.

AIKMAN, Rochester, N. Y.

TREATMENT OF ACUTE DIARRHEAL DISORDERS OF INFANCY AND EARLY CHILDHOOD WITH BANANA AND BANANA POWDER. E. W. BRUBAKER, J. Michigan M. Soc. **36**:40 (Jan.) 1937.

This paper deals with the clinical results in fifty-six children treated with banana or banana powder and twenty-four children used as controls, for whom the standard methods of treatment were used. The methods of treatment are described and the results are tabulated. It is the author's opinion that treatment with banana pulp or powder is more efficacious than older methods of treatment.

CAREY, Detroit.

IMPERFORATE ANUS. STANLEY J. SEEGER, Wisconsin M. J. **35**:960 (Dec.) 1936.

The estimated incidence of imperforate anus varies from 1 in 1,500 births to 1 in 10,000, according to different authors, but is probably more frequent than is reported. There are several variations of the anomaly. Six different types are discussed; reports of cases and diagrams are presented, and methods of determining the exact anatomic relationships and the results of surgical intervention are described. The embryonic development of the urogenitorectal region is reviewed, and Ombredanne's classification of anomalies in these parts is given. Rectovaginal communications in girls and recto-urethral fistulas in boys constitute the most frequent anomalies found.

Even in cases of complete occlusion there are usually no symptoms during the first twenty-four hours. Thereafter, increasing distention occurs, and death follows within a week or ten days unless there is surgical correction. Immediate operation is imperative when obstruction exists. This must be preceded by a careful anatomic study. It is surgically important to know that the sphincters are developed in connection with the perineum. Because of the presence of air in the bowel, roentgenograms taken with the infant in the inverted position show exactly the point at which the rectum terminates. A good functional end-result is apparently obtainable in most of these anomalies.

JANNEY, Wauwatosa, Wis.

HEPATOMEGALY WITH RETARDATION OF STATURAL GROWTH IN A DIABETIC CHILD. P. NOBÉCOURT, P. DUCAS and M. LAROCHE, Arch. de méd. d. enf. **39**:697 (Nov.) 1936.

Diabetes developed in a girl of 5 years, who had been in normal health up to the age of 2 years. With the exception of several severe attacks of hypoglycemia during this period, she exhibited all of the characteristics of juvenile diabetes, and her condition would merit no special attention but for certain unusual features. Among these were the precociousness of its onset, its appearance soon after a mild attack of chicken-pox, and the fact that the sugar content of the blood continued to be normal long after the usual clinical manifestations were noted.

The most striking departure, however, was the development of hepatomegaly, with corresponding abdominal enlargement, and retardation of skeletal growth, in the second year of the diabetes. The hypertrophy of the liver affected the entire organ; from normal size at the stage of invasion, it gradually augmented in volume until its lower border extended 3 fingerbreadths below the costal arch; its surface was smooth, hard and painless. There was apparently no involvement of the spleen, no ascites and no icterus. Functional tests were negative. With respect to height, the child measured, on first examination, 81.5 cm., the average for 2 years being 77.5 cm. This showed an excess at that age of 4 cm. At 4 years, her height was 93 cm., which also compares well with the accepted standard, but at 5 years she measured 95 cm., while the normal is 98. A brother of 3½ years was 99.5 cm. tall.

One finds, therefore, the association of pronounced hepatomegaly, abdominal enlargement and retardation of growth in a diabetic child treated with insulin which fits the description of a syndrome described by P. Mauriac and G. Mouriquand.

AMESSE, Denver.

MASSIVE FATTY INFILTRATION OF THE LIVER IN A CHILD. L. BABONNEIX, Gaz. d. hôp. **110**:66 (Jan. 13) 1937.

A child 5 years old was admitted to the hospital with diarrhea of a few days' duration and died there within a month. The only positive physical finding on admission was a large liver with a normal spleen. There was no fever. Later she contracted diphtheria and German measles. Autopsy showed fatty infiltration of the liver without evidence of cirrhosis.

KAJDI, Baltimore.

GASTRIC STASIS. J. LEVESQUE and S. DREYFUS, Nourrisson **25**:1 (Jan.) 1937.

Persistent vomiting occurs sometimes in infants who suffer neither from pylorospasm nor from pyloric stenosis. Ten cases in point are briefly described. The cause is thought to be subnormal sensitivity or lessened excitability of the gastric mucosa. The treatment is purely dietetic since these babies respond promptly to a regime of buttermilk or lactic acid milk.

MCCLELLAND, Cleveland.

REMARKS ON THE INSULIN TREATMENT OF PERIODIC VOMITING WITH ACETONEMIA. M. LELONG, Paris méd. **2**:344 (Nov. 7) 1936.

Lelong thinks that great care should be exercised in the use of insulin in cyclic vomiting. This is especially true in the initial stage when hypoglycemia is already present. Later when it is possible to check with determinations of the blood sugar there may be an occasion for its use. However, it is difficult to judge whether or not patients given dextrose and insulin, might not have done as well on dextrose and fluids alone. In all events insulin should be used only in conjunction with dextrose and never alone.

LESLIE, Evanston, Ill.

DIAPHRAGMATIC HERNIA OF THE STOMACH IN THE CHILD. R.-A. MARQUÉZY, M. TAVENNEC and S. HUGUET, Paris méd. **2**:350 (Nov. 14) 1936.

Diaphragmatic hernia of the stomach may go unrecognized for many years although the subject usually suffers from malnutrition and anemia. The prognosis, although better than for herniation of the colon through the diaphragm, is nevertheless grave. In infants and children, vomiting, ill-defined pain and poor appetite are the most constant complaints. There may be associated severe malnutrition and dwarfing, with marked anemia. The diagnosis is confirmed by the x-ray picture.

The anemia may be combated with iron and liver therapy, and often the nutrition may be improved by a position following meals which allows better emptying of the stomach. Surgical intervention, though not urgent, should be considered.

LESLIE, Evanston, Ill.

PNEUMOCOCCIC PERITONITIS. P. BROUSTET, Progrès méd., Nov. 21, 1936, p. 1809.

A full discussion of pneumococcic peritonitis is given. Of particular interest are the diagnostic aids and treatment. In encysted forms, aspiration of pus will clinch the diagnosis, and evacuation is indicated in treatment. In the intermediary stage spontaneous amelioration of generalized peritonitis indicates a pneumococcic type. Diagnosis in the initial stage is particularly important, because at this time, since there is no accumulation of pus, operation serves no purpose and may do definite harm. Generalized abdominal rigidity, vomiting and diarrhea are important points. A positive blood culture may also be obtained at this stage. If indications are not clearcut and appendicitis is seriously suspected, a small incision with the least possible disturbance of the abdominal content is all that should be undertaken unless the diagnosis of appendicitis is confirmed.

LESLIE, Evanston, Ill.

DISEASE OF THE PANCREAS IN INFANCY. B. BENASSI, Clin. pediat. **18**:728 (Nov.); 751 (Dec.) 1936.

This is a thorough-going review of the literature on the subject, which cannot be abstracted profitably.

DOOLEY, New York City.

ULCER OF THE DUODENUM IN A NINE YEAR OLD CHILD. F. MENNA, Pediatria **45**:60 (Jan.) 1937.

Menna describes duodenal ulcer associated with chronic appendicitis in a child 9 years old. Reviewing the literature, he emphatically states that cases of this type are rare up to the age of 12 years and that only few cases (a score or two) have been reported.

It is important to know that in the child the course of the disease is very similar to that in the adult and that it is not true that the diagnosis for a child is made only on the presence of melena or hematemesis.

He calls attention to the hereditary character of the lesion presented in the patient.

PALMIERI, Brooklyn.

TREATMENT OF INFANTILE DIARRHEA WITH SUBSTANCES EXTRACTED FROM HONEY. G. STANCANELLI, Riv. di clin. pediat. **34**:1053 (Nov.) 1936.

The therapeutic value of honey in the treatment of diarrhea is believed to be due to its content of malic acid, of tannic acid and above all of pectin. Stancanelli used an extract of honey in colloidal suspension in treating twenty infants with intestinal disturbances and parenteral diarrhea. The extract is preferable to the honey itself because the quantity of sugar given is less and because the product is available at any season of the year.

Of the twenty infants, fifteen showed complete cure and two a distinct improvement within from one to four days. In three children the gastro-intestinal symptoms were not improved. The better results were obtained in cases of acute and subacute dyspepsia. Fairly satisfactory results were obtained in cases of parenteral diarrhea associated with infections, such as grip or pertussis. The children with marked toxemia did not show much improvement.

HIGGINS, Boston.

INTESTINAL INFANTILISM. JOSE CHAGAS FILHO, J. de pediat., Rio de Janeiro **3**:542 (Dec.) 1936.

The child described was a girl 2 years of age. Her condition was kept under control by a diet of bananas. A further complication was ascariasis. An excellent discussion of the condition and a bibliography are given.

SANFORD, Chicago.

TREATMENT OF CELIAC DISEASE. G. LODI, Med. inf. **7**:325 (Nov.) 1936.

Lodi gives a case history, that of a twin, who at the age of 3 years began to show signs of disturbance of the gastro-intestinal tract and at the time of admission to the hospital at the age of 4½ years presented the classic picture of celiac disease. The child remained under observation over a period of two years, during which time various methods of treatment were used. Data are given regarding the growth of the child during this period.

In a review of the therapy of celiac disease the author divides the treatment into five fundamental divisions: (1) medicinal, as with pancreatic extract, insulin, bile salts, glandular extracts, blood transfusions, horse serum and clyses; (2) physical, as with ultraviolet rays, massage, hydrotherapy and intestinal lavage; (3) psychiatric; (4) climatic, as with a sojourn in the mountains; (5) dietetic, including the rise of high protein, banana, honey, low fat and high vitamin diets.

HIGGINS, Boston.

CELIAC DISEASE. M. PONTICACCIA, Med. inf. **8**:15 (Jan.) 1937.

Two children in the same family, one aged 12 and the other 10, showed signs of celiac disease, namely, enlargement of the abdomen, hepatomegaly, diarrhea and smallness of stature. Treatment was by means of honey and was successful. Speculation over the reason for the benefit of the honey treatment brought up the possibility of the results being due to (1) tannic acid, (2) malic acid, (3) pectin and (4) vitamins. No definite conclusions are drawn. HIGGINS, Boston.

LATENT (ANICTERIC) DIFFUSE HEPATOPATHY. H. KLEINSCHMIDT, Kinderärztl. Praxis **7**:489 (Nov.) 1936.

Three typical cases are reported as examples of a rather frequent disorder in childhood. Whenever abdominal pains which cannot be explained by abdominal findings occur in children who are free from infection and whose urine shows a reaction positive for urobilinogen, Kleinschmidt believes a condition exists that is due to what might be called very mild catarrhal icterus. A reaction positive for urobilinogen in the urine is characterized by a red color that appears without heating the urine after dimethylparaminobenzaldehyde (Ehrlich's aldehyde reagent) has been added. HEYMANN, Cleveland.

THE DIAGNOSIS OF TUMORS OF THE LIVER. FRIEDRICH LINNEWEH, Monatschr. f. Kinderh. **67**:422 (Dec.) 1936.

Dioxyacetone, having a composition of $C_3H_6O_3$, ranks as a sugar. In doses of from 15 to 25 Gm. dissolved in tea this drug is useful in the differential diagnosis of enlargements of the liver. In cirrhosis the amount of the substance present in the blood after a tolerance test will be above normal, while in von Gierke's disease examination of the blood following such a test will not reveal a trace. GERSTLEY, Chicago.

MEGACOLON AND CHRONIC APPENDICITIS IN CHILDREN. F. DEMMER, Wien. klin. Wchnschr. **49**:1366 (Nov. 6) 1936.

Three cases of interrelated megacolon and chronic appendicitis in children observed by Demmer began with attacks of abdominal pain, the result of severe obstipation. There were palpable swellings in the abdomen. Roentgen examination showed that the sigmoid was enormous (in one case, four times the normal size) and that obstruction existed. There was also evidence of chronic appendicitis, although whether this or the megacolon was the primary condition could not be determined; at any rate, their coexistence was plain.

In the first patient, an 11 year old boy, an operation was performed and the appendix removed. Surprisingly rapid recovery occurred. Previously the size of a 7 year old child, he showed marked physical improvement. Defecation became normal, and the sigmoid, untouched during the appendectomy, was reduced to two thirds of its former length.

In the second patient, a 5 year old boy, the appendix was removed, and the sigmoid, which had reached the edge of the liver, was shortened by segmentation and then rejoined end to end. Here, likewise, a rapid recovery took place.

In a third patient, a 3 year old girl, the attacks were relieved by hot water baths, which caused movement of the bowels.

Demmer recommends warm baths in the general treatment and, if the attack is acute, operation for appendicitis only, with the thought that this may remove the cause of the megacolon, as in his first example. However, Pässler's observations, which led him to ascribe megacolon to a sympathetic inhibition of peristalsis and Kirshner's successful operation on the ganglion to relieve obstipation show that other causes besides chronic appendicitis may exist. In fact, Demmer suggests that the basic cause of megacolon may be an inherited abnormality in the sigmoid, although he believes appendicitis is the immediate cause more often than is commonly supposed. ABT, Chicago.

CONGENITAL OBLITERATION OF THE SMALL INTESTINE. L. W. VAN OUWERKERK, Nederl. tijdschr. v. geneesk. **80**:4992 (Nov. 7) 1936.

In connection with six cases of congenital narrowing or obliteration of the small intestine observed in the Coolsinge Hospital, Rotterdam, this abnormality is submitted for discussion. It is not so rare as one is apt to assume. Early surgical treatment is pointed out as the only measure that gives an outlook to recovery, though limited, as four of the six children who were operated on died.

VAN CREVELD, Amsterdam, Netherlands.

## Nervous Diseases

HYPERPYREXIA INDUCED BY HYDROTHERAPY IN THE TREATMENT OF CHOREA. H. LOWENBURG SR. and S. NEMSER, Arch. Pediat. **53**:722 (Nov.) 1936.

The report concerns itself with hydrotherapy as a means of producing hyperpyrexia in a patient with chorea. The procedure is simple and effective. The patient is placed in a tub filled with water at from 90 to 95 F. Every effort is made to avoid fear and shock. The temperature of the water is gradually increased to and maintained at 120 F. The patient remains in the bath for from two to three hours. The temperature is taken at intervals of fifteen minutes; it should reach 103 F. or higher at the end of thirty minutes and should remain at this level throughout the duration of the treatment. The bath is given before a meal or several hours after a meal. Fluids are given to the patient, and cool cloths may be wrapped around the patient's head during treatment. If resistance is encountered, or if the patient reacts poorly, he is removed immediately. Following the bath, the temperature is read at frequent intervals until it returns to normal. At first, baths are given daily; then the interval between baths is gradually increased. Twelve or slightly more baths are usually sufficient.

The authors report three cases in which a favorable response was shown to this type of treatment.

ORR, Buffalo.

PYKNOLEPSY: REPORT OF A CASE. A. CAPPER, Arch. Pediat. **53**:740 (Nov.) 1936.

Capper describes a case of pyknolepsy which had its onset in a girl at the age of 7 years. The condition existed over a period of six and one-half years with as many as a hundred seizures daily. The attacks did not increase in severity. There was no aura, and during an attack no clonic or tonic spasms occurred. She recollected each attack and frequently could be stopped in the middle of one. Phenobarbital and its derivatives failed to give relief.

The attacks ceased when the patient reached full puberty. Since then, a period of eighteen months, she has had no seizures.

ORR, Buffalo.

ANGIOMA OF THE LEFT BRACHIUM PONTIS WITH ASSOCIATED ANEURYSMAL VARICES. C. L. DALE and C. B. COURVILLE, Bull. Los Angeles Neurol. Soc. **1**:88 (June) 1936.

A boy aged 9 years was seized suddenly with headache, stupor and vomiting, shortly after playing ball. Half an hour later he could not be aroused; the pupils were fixed; the pulse rate was 120, and the spinal fluid was extremely bloody. Death occurred after a few hours. He had recovered from a similar attack two years before. Necropsy revealed dilated thin-walled veins in the left lateral fissure and along the left side of the pons. On section the left brachium pontis was observed to contain a large number of dilated veins, which had produced marked atrophy of the fibers of the middle peduncle and reduction in size of the left lobe of the cerebellum. No clinical evidence of cerebellar dysfunction had been noted during life.

MACKAY, Chicago. [ARCH. NEUROL. & PSYCHIAT.]

TREATMENT OF SYDENHAM'S CHOREA WITH TYPHOID-PARATYPHOID VACCINE. D. WEISMAN and C. LESLIE, New York State J. Med. **36**:1587 (Nov. 1) 1936.

Fifty cases of chorea are reported in which New York City typhoid-paratyphoid vaccine was used intravenously to produce hyperpyrexia. The occurrence of a chill was taken as indicating a rapidly rising temperature. The temperature was then taken every five minutes until the mounting hyperpyrexia was over. Sodium amytal was given two hours before treatment to make the children more comfortable during the period of high temperature. The treatment is described in detail. Ninety-two per cent were cured, and there were no ill effects. Ten per cent had recurrences in from one to three years. AIKMAN, Rochester, N. Y.

FAMILIAL SCHILDER'S DISEASE. A. MEYER and T. TENNENT, Brain **59**:100, 1936.

Cases of familial Schilder's disease have been reported by Krabbe (1916), Scholz (1925) and Collier and Greenfield (1924). Meyer and Tennent report on an interesting family in which two brothers, aged 4 and 9 years, presented characteristic clinical findings and pictures of the disease at autopsy. The mother and father were alcoholic. There were three brothers. In the two cases of Schilder's disease there was an antecedent history of jaundice and severe gastro-intestinal symptoms. Two other children had had gastro-intestinal symptoms, but only one of them showed nervous symptoms, in the form of slight ataxia. The fifth child is normal in all respects at present. The mother, aged 37, shows evidence of progressive spinal disorder, suggesting disseminated sclerosis. The onset of her nervous symptoms followed that of the symptoms in her children.

The pathologic changes in cases of familial Schilder's disease do not necessarily correspond closely. However, in the two cases reported the similarity in the distributions of the pathologic lesions is striking. The frontal lobes were preserved as a whole. The changes increased rapidly posteriorly until they involved all the white matter. The process was nearly symmetrical. In both cases there was preservation of the basal ganglia and cerebellum. In the affected areas there was severe infiltration of the vessels with plasma cells and lymphocytes, which penetrated into the parenchyma.

Meyer and Tennent suggest the possibility of an extracerebral factor as the cause of Schilder's disease (Ferraro, 1928, and Macnamara and Dickson, 1933). Greenfield (1933) had something similar in view when he suggested that in his cases of infantile progressive sclerosis there was a supply of abnormal lipoids. Globus (1932) expressed the belief that an onset with gastro-intestinal symptoms is frequent in Schilder's disease. Gastro-intestinal disturbances not only preceded the neurologic symptoms in the two cases of Schilder's disease described by Meyer and Tennent but were recorded in the history of two other children in the family.

In both cases there was irregular demyelinization of the optic chiasm, extending to the optic nerves. In coronal sections in both cases, the peripheral and more particularly the ventral part of the optic tract was better preserved than the central and upper parts. Fat stains showed the process to be the same as that in the cerebral white matter. At the zone of demarcation was a layer of fat-laden globoid cells, indicating that the lesion was proceeding from the center toward the periphery. Monnier and Walthard (1934) described similar centrally placed lesions of the optic tract in a case of cerebral syphilis in which the anterior choroid artery supplying a part of the optic tract was obliterated. This may indicate a vascular origin of the changes in the optic tract in cases of Schilder's disease.

There was no systematic limitation of the lesion to functional units, although it is obvious that, according to the scheme of Brouwer and Zeeman (1923 and 1926), the papillomacular bundle must have suffered first and to the greatest degree. Equally interesting is the striking similarity of the lesions of the optic tract to those observed by Scherer (1932) in the well known disease in monkeys; the lack of peripheral optic lesions in Schilder's disease was one of the reasons that Schob (1931) and Spielmeyer (1931) did not accept a close relationship between these conditions. Furthermore, gastro-intestinal disturbances, so out-

standing a feature in the disease in monkeys described by Schob and Scherer, are not foreign to Schilder's disease. The similarity applies to honeycomb lesions in the spinal cord of monkeys, which suggested to Scherer a condition related to pernicious anemia. Honeycomb lesions occur in Schilder's disease (Wertham, 1932, and Marinesco, 1930), and they might be seen more frequently if more attention were paid.

Histologic similarities do not necessarily indicate a close etiologic relationship. Moreover, since Schilder's disease is not likely to be a disease entity, changes in one of its groups need not apply to another. The fact, however, that an apparently epidemic and transmissible disease (Gaertner, 1932 and 1933) and Schilder's disease of heredofamilial nature have much in common presents an interesting pathogenic problem requiring further attention.

SALL, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

STREPTOCOCCAL MENINGITIS FOLLOWED BY RECOVERY. J. McQ. THOMAS, Proc. Roy. Soc. Med. **30**:411 (Oct.) 1936.

A case is reported in a boy of 7 years. In April 1936 he had had scarlet fever followed by otitis media. Paracentesis on the right side and incision of a postauricular abscess on the left side were performed. Since then he has had paralysis of the left side of the face. In the middle of September he was admitted to the hospital with a history of vomiting, fever, drowsiness and earache for the past three days. At the beginning of October cortical mastoidectomy was performed on the right side. Ten days later cortical mastoidectomy was performed on the left side, but no pus was found in the antrum. Lumbar puncture showed turbid fluid under normal pressure. Culture showed no growth. There were 6,000 cells per cubic millimeter and most of them were polymorphonuclears. A week later a few gram-positive diplococci were found. A derivative of sulfanilamide, prontosil soluble (the disodium salt of 4'-sulfamidophenyl-2-azo-7-acetylamino-1-hydroxynaphthalene-3, 6-disulfonic acid) was given, 3 tablets a day. The temperature fell and the symptoms disappeared. The administration of the drug was continued for one week. A month later lumbar puncture revealed normal fluid under normal pressure. The Wassermann reaction of the fluid was negative.

WILLIAMSON, New Orleans.

TUMORS AT THE BASE OF THE BRAIN IN CHILDREN. R. A. KHERSONSKY, B. G. ROUBINSTEIN and K. S. WINER, Arch. de méd. d. enf. **39**:707 (Nov.) 1936.

Cerebral tumors among children represent a relative frequency of from 4 to 8 per cent of the total number reported, according to Cushing and his associates. Among these neoplasms, tuberculomas occupy the first place and gliomas the second; with respect to localization, in most cases a tumor of the brain in early life occupies the posterior fossa while a glioma in most cases is found in the cerebellum.

In this contribution from the staff of the Psychoneurologic Institute and the Anatomopathologic Institute of Odessa, four tumors are reported, three of these representing glioblastoma and one ganglioneuroma.

The clinical observations are offered in detail, together with an extended discussion of the evolution and the progress in each instance to a fatal issue. Surgical intervention in these cases presents such enormous difficulties that the authors feel an earlier diagnosis and the exhibition of radiotherapy offer the only hope for successful treatment.

AMESSE, Denver.

ELEVEN CASES OF CONGENITAL DISTURBANCES OF THE CRANIAL MOTOR NERVES IN ONE FAMILY. A. H. FORTANIER and N. SPEIJER, Encéphale **31**:252, 1936.

The disease considered here was first described by Moebius as *infantiler Kernschwund* and was attributed to prenatal degeneration of the nuclei of the cranial nerves. Three types have been described, depending on the nerves involved.

The first type involves only the territory of the oculomotor nerve, and the second, that of the facial nerve and sometimes the sensory or motor territory of the trigeminus nerve and/or the acoustic nerve. In only one case was there any disturbance of lacrimal secretion (Zappert). In the third type only the hypoglossus and glossopharyngeus nerves are involved. These disturbances are generally hereditary and seem to be dominant. In some cases other congenital anomalies, particularly spina bifida, are present. In some families there are also psychoses.

The family reported here consisted of sixty-eight persons. Information is given on five generations. Deafness was the only defect known in the first two generations — congenital deafness on one side and deafness following typhoid in the father and brother of the maternal progenitor, who was not herself deaf. Yet she, as well as her sister, who married a man with no known hereditary defect, had offspring with the disease. In four cases there were lacrimal disturbances. The other defects, which were present alone or in combination, were congenital facial paralysis, congenital deafness and spina bifida. There were no psychoses. In several patients examined there were only latent disturbances of the motor nerves, such as excessive sensitivity of the trunk of the facial nerve to galvanic stimulation. There were no known psychoses. The factor of heredity is certain in this family. The mode of transmission can be explained only as that of an irregular dominant trait; that is, in some persons the trait is recessive. This would explain, among other things, the presence of latent disturbances, revealed only by electrical examination. One member of the last generation, in addition to congenital bilateral facial palsy, deafness and absence of lacrimal secretion, presented excessive brachycephaly, epicanthus, deviation of the little finger and congenital paralysis of both lower extremities, which, however, improved with age. The intellect was normal. The motor disturbances may perhaps be considered as an abortive form of Oppenheim's amyotonia congenita. The heredity in this case is obscure.

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

CLINICAL AND PATHOLOGIC REVIEW OF SEVERAL CASES OF TUMOR OF THE BRAIN. U. AVELLONE, Arch. ital. di pediat. **4**:580 (Dec.) 1936.

This is a detailed clinical and pathologic report on a cerebral gliosarcoma, a pontile glioma and multiple tuberculomas in the cerebellum and left lenticular nucleus, all occurring in children.

DOOLEY, New York.

SYNDROME OF PYKNOLEPSY. U. SENIN, Med. inf. **7**:293 (Oct.) 1936.

Two children, 6½ and 7 years old, are discussed. They had minor neurologic attacks, which Senin classified as pyknoleptic. One of the children was treated with bromides, phenobarbital and a ketogenic diet without relief; then injections of ephedrine hydrochloride were given for eleven days, the attacks ceasing in two days and not recurring after the injections had been discontinued. The rationale for the giving of ephedrine was a possible relationship between narcolepsy and pyknolepsy. The second child got complete relief following an intensive course of phenobarbital with a ketogenic diet.

Statistics are quoted showing the prognosis of pyknolepsy in 166 children treated in various ways; 52 (31 per cent) were cured; 34 (20 per cent) later presented definite epilepsy, while 80 (48 per cent) showed no change.

[The attacks as described would be diagnosed as petit mal in American clinics. In interpreting this paper "pyknolepsy" and "petit mal" may be regarded as synonymous.—Abstractor.]

HIGGINS, Boston.

ACUTE CEREBRAL TREMORS. A. VALLEJO NAGERA, Paidoterapia **15**:101 (June) 1936.

Vallejo Nagera presents a case of acute cerebral tremor, a rare form of encephalitis, in a 9 month old child, which is of special interest as only twenty-four such cases have been reported. The condition occurs in the first year of

life and often follows an acute infection. The tremor was noted in all four extremities and the head but disappeared when voluntary movements were attempted, and it was accompanied by epileptiform convulsions. Death occurred suddenly.

HERRON, Spokane, Wash.

MIXED INFECTION OF THE MENINGES WITH KOCH'S BACILLUS AND FRIEDLÄNDER'S PNEUMOBACILLUS. D. v. MÓRITZ, Arch. f. Kinderh. **109**:21, 1936.

A case is reported.

CRANE, Washington, D. C.

CARCINOMA OF THE CHOROID PLEXUS WITH UNUSUAL CLINICAL MANIFESTATIONS. N. ZDRAHAL, Arch. f. Kinderh. **109**:24, 1936.

A case is reported. Three illustrations are given.

CRANE, Washington, D. C.

CHVOSTEK'S PHENOMENON WITHOUT SPASMOPHILIA DURING THE FIRST TWO YEARS OF LIFE. H. KLEINSCHMIDT, Kinderärztl. Praxis **7**:537 (Dec.) 1936.

This is a report on two infants, 9 and 11 months of age, who had the Chvostek sign. Lack of rachitic symptoms, a normal content of calcium in the blood and the fact that the infants were observed in July and August make the diagnosis of tetany extremely unlikely. The Chvostek sign in infancy can also be due to a hyperexcitable nervous system, and its presence does not prove beyond doubt that tetany is present.

HEYMANN, Cleveland.

CLINICAL STUDIES OF ACUTE PRIMARY ENCEPHALITIS. M. SILBERMANN and ZAPPERT, Wien. klin. Wchnschr. **49**:1577 (Dec. 25) 1936.

Silbermann and Zappert investigated encephalitis in its various forms in 200 patients ranging in age from 1½ to 60 years.

Two questions were considered in the research: 1. In what proportion of these patients was the encephalitis of the acute primary type ("lethargic" or "Economo's" encephalitis)? 2. What are the clinical symptoms of primary encephalitis in general?

The primary type was observed certainly in only 7 and probably in 3 other cases—an incidence of 5 per cent. In these cases it was characterized not only by a peculiar lethargy and ophthalmoplegia but by sleeplessness, parkinsonism, change in character and tics or muscle spasms.

Of the non-Economo encephalitis there were many types (not to mention that in a few cases the condition fitted into no classification): (1) with loss of consciousness, (2) with nonlocalized cerebral symptoms, (3) with hemiplegia, (4) with acute cerebral tremor, (5) with symptoms of disturbance of the cerebral nerve centers and of the cerebellum (encephalitis pontis et cerebelli), (6) with cerebral and spinal symptoms and (7) with unmistakable meningeal symptoms.

In all cases the disease was characterized by acute fever and cerebral symptoms, which appeared early in the course of the illness. It was not always possible in the clinic to distinguish between encephalitis and a tumor of the brain or poliomyelitis. The latter, in fact, seems to have a close relationship to encephalitis, as appears from the following case histories: Two children were vaccinated against smallpox simultaneously. In one typical postvaccinal encephalitis developed; in the other, unmistakable meningitis serosa. Since there was no poliomyelitis in the neighborhood, the only possible explanation for the two reactions seems to be that the meningitis and the encephalitis were manifestations of a common infection resulting from the vaccination.

In several cases of hemiplegic encephalitis in children there was a direct relationship to a previous lesion of the brain.

ABT, Chicago.

## Psychology and Psychiatry

INTELLIGENCE RATING OF THE ALLERGIC CHILD. G. PINESS, H. MILLER and E. B. SULLIVAN, J. Allergy **8:** 168 (Jan.) 1937.

The intelligence rating of 145 children attending the clinic for patients with allergy at the Children's Hospital in Los Angeles was compared with that of children attending the schools of that city. The age of the allergic children ranged from 5 years and 5 months to 15 years and 4 months. The conclusions are:

1. The asthmatic group is very similar in intellectual level to a normal group with the variation of a normal group. It includes children of superior, average, normal and inferior intelligence.

2. There might be some indication that the incidence of allergy is less in the feebleminded group, but the data available are very general and not statistically reliable.

3. As far as progress in school is concerned, the group with allergy is similar in grade placement to the normal group.

4. There is evidence in the allergic group of slightly more retardation in school than would be expected if their illness had not handicapped them.

HOYER, Cincinnati.

TRENDS IN CHILD PSYCHIATRY. E. WOLFF, J. Pediat. **10:**90 (Jan.) 1937.

Wolff reviews the present activity of the child guidance clinic and pediatric-psychiatric service, describing in detail the organization and the method of approach in various centers. Certain important changes in the development of child psychiatry have taken place in recent years, notably that child psychiatric services have been established within pediatric departments. Here behavior problems are handled, together with all other problems of children. The accent in child psychiatry has shifted, as it has in medicine generally, from treatment to prevention. The writer believes that the pediatrician's service should be the main factor in the prevention and treatment of behavior problems in childhood.

RAUH, Cincinnati.

MONGOLISM OCCURRING IN AMERICAN INDIANS: REPORT OF THREE CASES. J. SIRKIN, New York State J. Med. **37:**167 (Jan. 15) 1937.

Mongolism has not previously been reported in American Indians. Serkin reports the condition in Indians in the Newark (N. Y.) State School. The mother of one of these children, a 9 year old girl, was 47 years of age at the time of the patient's birth. The other two patients were brothers. The first was born when the mother was 39 and the other when she was 40 years of age.

AIKMAN, Rochester, N. Y.

INFLUENCE OF EMOTIONAL SHOCK ON THE PSYCHE OF CHILDREN. G. PAUL-BONCOUR and G. NÉRON, Progrès méd., Jan. 2, 1937, p. 9.

This is an exceedingly thoughtful discussion of the harm that may come to children through emotional disturbance. The shock need not be a sudden one or anything of import to the adult judgment, but careless and exaggerated conversations over monetary or marital difficulties, punishments and highly emotional moving pictures may cause profound alterations in the child's attitude toward life. Numerous examples of such occurrences are given. In some, the direct cause is easily found; in others, it must be searched for carefully. The constitutional make-up of the child is an important factor. Scenes which will slide off one child will make long-lasting impressions on another. An appreciation of these facts by parents might obviate much unhappiness.

LESLIE, Evanston, Ill.

SOCIAL ADAPTATION OF PERSONS WITH ABNORMALITIES OF INTELLIGENCE AND CHARACTER. G. HEUYER and S. HORINSON, Rev. méd.-sociale de l'enf. **5**:1 (Jan.-Feb.) 1937.

Heuyer and Horinson in this report review the handling of 500 patients by the Clinical Annex of the Juvenile Neuropsychiatric Clinic. After these patients had been submitted to a thorough medical and psychiatric study they were given some choice in the type of placement which was to be arranged for them. The results of the attempted readjustment were correlated with the patients' intelligence, and it was found that the greatest success was obtained in the patients with the highest intelligence. From another standpoint, the patients who were given agricultural rather than urban placement were helped the most. In all, the authors felt that 68 per cent of their subjects had been helped.

DIETRICH, Los Angeles.

THE FAMILY AND SOCIAL ENVIRONMENT OF THE DELINQUENT CHILD. G. BAILA, Rev. méd.-sociale de l'enf. **5**:28 (Jan.-Feb.) 1937.

In developing the thesis that environmental factors rather than fundamental unworthiness of parents are usually responsible for delinquency in children Baila stresses, of course, the effects of poverty. The rôle played by unsettled parental marriage relationships, alcoholism, difficulties at school and the temptations of the city streets are reviewed without contributing any new thoughts on the subject.

DIETRICH, Los Angeles.

CHILD PSYCHOLOGY FOR THE PRACTICAL PHYSICIAN. F. HAMBURGER, Med. Klin. **33**:3 (Jan. 2) 1937.

The importance of the influence of the mind on the body is emphasized. Happiness leads to capillary dilatation and energizes the child to muscular activity which in turn accelerates metabolism and increases the demand for food. The mother's disposition or mood has an important influence on the child. A child's relations with persons with whom he comes in contact (especially with the mother) must be considered. Anorexia is almost entirely on the basis of an aphysiologic and unpsychologic attitude on the part of the mother or of the child's attendant. A child should not be coaxed or forced to eat. "Hunger is the best cook." Undernutrition as well as overnutrition may be the result of habit. In the nutrition of new-born infants, too rigid insistence on regulations should be avoided. Undesirable habits are best corrected by disregarding them. Ineffective attempts at correction may establish them more firmly.

SIEMSEN, Chicago.

THE RELATION BETWEEN RICKETS AND MENTAL DEFICIENCY. T. BRANDER, Monatschr. f. Kinderh. **69**:47 (Feb.) 1937.

This is a psychologic and psychiatric study of 375 premature children aged from 7 to 15 years. It was found that in a general way the more severe the signs of healed rickets the greater was the frequency of mental retardation which varied from mere stupidity to imbecility. The greater the rachitic residue the lower was the general average of the intelligence quotient for all the children. In the majority the defects of intelligence were relatively mild, so that rickets should not be considered as of practical significance in the etiology of oligophrenia. Brander does not claim that the associated mild mental defects are necessarily due to rickets. Both conditions may be due to a deeper cause. There is no question that mental retardation predisposes to rickets.

GERSTLEY, Chicago.

RELATION BETWEEN ENLARGED TONSILS AND MENTAL DEFICIENCY. T. BRANDER, Monatschr. f. Kinderh. **69**:57 (Feb.) 1937.

In 373 premature children aged from 7 to 15 years Brander found that the incidence of mental retardation occurred parallel to the degree of tonsillar hyper-

plasia. The greater the hyperplasia the lower was the general average of the intelligence quotient. The defects of intelligence being of relatively mild degree, the tonsillar hyperplasia cannot be considered a factor of oligophrenia.

Brander does not claim that the associated mild mental defects are necessarily due to the fact that the tonsils are enlarged. In the presence of large tonsils the symptoms of the more defective children seem to be accentuated. Perhaps enlargement of the tonsils and mental retardation have a common cause. Removal of tonsils may help some children, but it is valueless in such conditions as oligophrenia.

GERSTLEY, Chicago.

## Diseases of the Genito-Urinary Tract

GONORRHEAL VULVOVAGINITIS OF CHILDREN. K. J. KARNAKY, Arch. Pediat. **54**:34 (Jan.) 1937.

Two hundred children with vulvovaginitis were treated with tablets of acidulated sugar, with the same results as were experienced in the use of ovarian hormone. A favorable response to the therapy is not noted until the reaction of the vaginal secretions reaches a $p_H$ of 5.5 or lower. On continuous use of the tablets the $p_H$ reached 4, the normal $p_H$ of the adult vagina.

A description of the tablet and the results obtained have been given by Karnaky in a previous publication.

ORR, Buffalo.

URETERAL TRANSPLANTATION IN THE VERY YOUNG. W. E. LOWER, Cleveland Clin. Quart. **4**:23 (Jan.) 1937.

Transplantation of the right ureter into the rectosigmoid was performed successfully in a boy with exstrophy of the bladder at 4 months of age.

MILLER, South Bend, Ind.

HYPERPARATHYROIDISM IN KIDNEY DISEASE. W. J. HIGHMAN JR. and B. HAMILTON, J. Clin. Investigation **16**:103 (Jan.) 1937.

Samples of blood from thirty-eight normal and twenty-six nephritic persons when examined by the method of Hamilton and Schwartz gave evidence of increased activity of the parathyroid glands in chronic renal disease. It is suggested that this increase constitutes a biologic defense against impending hypocalcemia secondary to retention of phosphates.

GUEST, Cincinnati.

NONOPERATIVE (GONADOTROPIC) TREATMENT OF CRYPTORCHISM. H. R. RONY, M. Clin. North America **21**:207 (Jan.) 1937.

Under normal conditions the testicles descend from the abdominal cavity to the scrotum during the seventh to eight month of intra-uterine life. The important factor in this migration is probably the maternal gonadotropic hormone. When delayed until puberty, descent is probably the result of the action of the gonadotropic hormone of the hypophysis of the boy.

Histologically the undescended testicle, prepubertal or postpubertal, shows absence of normal germinal epithelium in the seminiferous tubules as does the normal prepubertal scrotal testicle.

Evidence in favor of the specificity of gonadotropic therapy in cryptorchism justifies its careful clinical trial. Obviously it will not bring about descent of a testicle held up by mechanical obstruction. The optimal time for such treatment appears to Rony to be at the normal beginning of puberty—i. e., at the age of from 11 to 13 years.

EUGENE SMITH, Ogden, Utah.

URINARY ALKALINITY IN YOUNG CHILDREN AS INFLUENCED BY DIET AND DISEASE. FRANK C. NEFF, ROBERT C. FREDEEN, DAVID T. LOY and GEORGE V. HERRMAN, South. M. J. **29**:1213 (Dec.) 1936.

Dietary alkalinization of the urine, either as a substitute or as an adjuvant to drugs, is feasible in acute pyelitis. An infant having acute pyuria uninfluenced by diet or drugs probably has an inaccessible and diffuse type of renal infection accompanied with sepsis.

Grape juice was found to be preferable to the juices of other fruits in alkaline therapy.

SCHLUTZ, Chicago.

RENAL RICKETS. N. L. PRICE and T. B. DAVIE, Brit. J. Surg. **24**:548 (Jan.) 1937.

This article is based on the case report of a boy aged 14 who died of renal rickets. On postmortem examination the kidneys, which were greatly reduced in size, presented microscopically a general effect of advanced renal sclerosis. The parathyroid glands showed considerable hyperplasia.

A résumé of the clinical, chemical and roentgenographic bone changes and pathologic features is given.

The pathogenesis is not known, but two theories have been advanced: the renal theory and the endocrine theory. The renal theory is that owing to a chronic renal disease in childhood there has developed a condition of rickets with deformities and changes in the skeletal system, this being due to the inability of the damaged kidney to effect adequate excretion of phosphates. The parathyroids apparently hypertrophy in an endeavor to correct the hyperphosphotemia which is mainly responsible for the metabolic embarrassment. As this theory does not account for the early dwarfism an endocrine basis has been assumed. This presumes that there has been primary overactivity of the parathyroid glands with or without overriding pituitary dysfunction. The renal changes, according to this theory, are secondary. The chronic interstitial nephritis present is produced by excessive excretion of calcium which occurs in hypercalcemia due to hyperparathyroidism. This theory explains a number of factors but does not explain the group of cases in which the renal damage is secondary to a congenital anomaly of the urinary tract.

SUMMERFELDT, Toronto, Canada.

ECTOPIA VESICAE TREATED BY IMPLANTING URETERS INTO THE BOWEL. HAMILTON BAILEY, Proc. Roy. Soc. Med. **30**:158 (Dec.) 1936.

The ureters were implanted into the pelvic colon of a child of 2½ years by Coffey's third technic. The child thrived, and there was no evidence of infection of the urinary tract. He had about five motions a day.

WILLIAMSON, New Orleans.

PYELO-URETEROCYSTITIS IN EARLY INFANCY ASSOCIATED WITH MALFORMATIONS OF THE URINARY TRACT. E. LESNÉ, C. LAUNAY and P. CARREZ, Arch. de méd. d. enf. **40**:5 (Jan.) 1937.

The rôle of congenital malformations of the urinary tract in the production of pyelonephritis and cystitis in infants has been stressed chiefly by English and American observers, the majority of French clinicians offering but brief mention. Autopsies revealing the site and the nature of the principal deviations have complemented examinations of living subjects by methods ordinarily applied to older children and adults. A report made in 1924 by Bugbee and Wollstein on 4,903 necropsies of nurslings and young children showed urinary malformations in 2.3 per cent. Various other observations are reviewed. The authors discuss three instances of congenital malformation in a series of seven patients who succumbed to urinary infection. The first case concerned a boy of 10 months who was

admitted to the hospital with irregular temperature and urine with large numbers of pus cells; the colon bacillus was demonstrated. In spite of intensive treatment, including the use of a specific vaccine and transfusion, the patient steadily lost ground and died during the sixth week. Postmortem examination revealed enormous dilatation of both ureters, with segmentation and valvulation of the right, producing marked obstruction. There was also stenosis on each side at the point of entrance into the bladder.

The second case was that of a girl aged 1 year, with the usual signs of spasmophilia and pyelitis, who died suddenly, probably from laryngospasm. The autopsy showed a single kidney with a ureter dilated in the superior portion and stenosed in the lower to the extent that the finest probe could not be introduced.

The third observation was that of an infant of 3 weeks. Examination showed edema of the lower limbs and of the perineum, with a globular swelling in the lower part of the abdomen. A catheter withdrew 200 cc. of urine containing pus and a mixed bacterial flora. The edema promptly disappeared but recurred on the following day. Roentgenograms, made on the supposition that the baby was suffering from a vesical calculus, showed none. Retention continued for four months with daily catheterization; there was gradual loss of strength and weight until demise. Autopsy was not permitted.

AMESSE, Denver.

A CASE OF LIPOID NEPHROSIS. URBANO FREITAS, J. de pediat., Rio de Janeiro **3**:565 (Dec.) 1936.

A case of lipoid nephrosis in a girl aged 9 years is reported. The usual methods were tried, and variable results followed. The pathologic picture of the condition is discussed.

SANDFORD, Chicago.

FINAL OUTCOME OF GLOMERULONEPHRITIS IN CHILDREN. S. STEFANINI and G. TAROZZI, Med. inf. **7**:363 (Dec.) 1936.

Fifty-nine patients who had had acute glomerular nephritis were reexamined from two to thirty-one years after their illness. Only three of the patients had albuminuria; in two of the three it was orthostatic. No patients had nephrosis or renal sclerosis.

In twenty-nine of the fifty-nine patients there was increase in the size of the heart to the left, indicating some enlargement of the left ventricle. In many of these cases a definite increase in blood pressure, both systolic and diastolic, was present.

HIGGINS, Boston.

CHANGES IN THE SHAPE AND SIZE OF THE HEART IN KIDNEY DISEASE. L. UDVÁRDY, Fortschr. a. d. Geb. d. Röntgenstrahlen **54**:559 (Dec.) 1936.

Although the patients reported on in this paper are adults, the most important one of the conclusions of the study is applicable to children: "In acute glomerulonephritis we found that most of our patients presented an acute dilatation of the heart, which appeared suddenly and vanished with equal rapidity, leaving no traces." Changes in the roentgen aspects of the heart in other varieties of renal disease are also discussed. The bibliography is particularly useful.

McCUNE, New York.

PATHOGENESIS OF NEPHROSIS. L. P. DANIELS, Nederl. tijdschr. v. geneesk. **81**:289 (Jan. 23) 1937.

A young man of 18 years had acute glomerulonephritis as a result of an infection. Grave albuminuria led to hypoproteinemia with extensive hydropic swelling. The hematuria which was present at the onset diminished and vanished after some time, so that only the syndrome of nephrosis could be found. The ordinary treat-

ment of edema remained resultless. Therefore calcium, irradiated ergosterol and parathyroid were prescribed, whereupon the edema disappeared, while the hypoproteinemia remained. Some time afterward hypertension developed, and then general hemorrhages. Death was caused by a cerebral hemorrhage. The nephritis in this case was seen as a disease of capillaries (*capillairopatia*) and the symptoms of nephrosis as caused by the nephritis. Govaerts' ideas are discussed.

VAN CREVELD, Amsterdam, Netherlands.

## Diseases of the Ductless Glands; Endocrinology

EMOTIONAL AND INSTINCTUAL FACTORS IN DIABETES MELLITUS. G. E. DANIELS, Am. J. Psychiat. **93**:711 (Nov.) 1936.

Clinical and experimental evidence of a relationship between emotions and carbohydrate metabolism has long been recognized. This paper deals with an analysis of twenty-three diabetic persons ranging in age from 15 to 55 years. The neurotic manifestations varied in nature and degree—reactive depressions, anxiety neurosis, etc. In practically every instance there appeared a connection, direct or indirect, between the physioneurotic state and the diabetes.

JAHR, Omaha.

EFFECTS OF CHRONIC IMPLANTATION OF RATS WITH PITUITARIES OF THE SAME SPECIES. P. A. KATZMAN, N. J. WADE and E. A. DOISY, Endocrinology **21**:1 (Jan.) 1937.

It has been shown that there is a loss of sensitivity to hypophysial extract in animals after chronic administration of the extract. The cause of this insensitivity is at present controversial. The two chief explanations which have been advanced hold that the refractoriness is due to (1) antihormones and (2) antibodies.

Feeling that the validity of the antihormone theory depends on demonstrating the production of insensitivity in animals that are chronically treated with pituitary hormones of homozoic animals, the authors injected 1 or 2 hypophysial anterior lobes of rats daily into each of fifteen rats. With some of the rats this was continued for as long as nine months, and when the animals were put to death they still had enlarged ovaries. No evidence was obtained for the presence of gonadotropic or thyrotropic inhibitory substances in the plasma of these rats. On the contrary, this plasma augmented the gonadotropic response of immature female rats to implanted lobes. The weights of the adrenals, thyroids and hypophyses of the animals receiving the chronic treatment did not differ significantly from those of normal rats.

JACOBSEN, Buffalo.

SITE OF FORMATION OF THE POSTERIOR LOBE HORMONES. C. FISHER, Endocrinology **21**:19 (Jan.) 1937.

One of the unsolved problems of endocrinology, one that has persistently defied the attacks of many investigators, has been that of the site of formation of the hypophysial posterior lobe hormones—whether in the pars nervosa, pars tuberalis or pars intermedia.

In Fisher's experiment four atrophic posterior lobes of cats with diabetes insipidus were subjected to assay for their melanophore-expanding activity on live frogs. The results indicate that in diabetes the pars intermedia is physiologically active as well as histologically intact. The conclusion is therefore drawn that the pressor, antidiuretic and oxytocic activities in glands of the same type as those used in this study are correlated with degeneration of the pars nervosa and that the latter must play a rôle in the elaboration of these activities.

The results are discussed with reference to the various theories of the formation of the posterior lobe hormones.

JACOBSEN, Buffalo.

EXPERIMENTAL STUDIES OF THE ANTERIOR PITUITARY: IV. THE REPLACEMENT CAPACITY AND THE NON-CYCLIC BEHAVIOR OF HOMOPLASTIC ANTERIOR PITUITARY GRAFTS. M. SCHWEIZER, H. A. CHARIPPER and H. O. HATERIUS, Endocrinology **21**:30 (Jan.) 1937.

Experiments proved that after intra-ocular implantation in the pupillary margin of the iris, and after extra-ocular implantation in the lateral subconjunctival tissues, in a completely hypophysectomized guinea-pig the anterior lobe of the pituitary becomes dominantly basophilic and retains its gonadotropic capacity. The ovaries become progressively more follicular until after approximately two months a condition of constant estrus supervenes. The ovarian effect is exclusively a follicle-stimulating one, with complete absence of luteinizing influence.

The conclusions are that the grafts are functional in maintaining the ovaries in the follicular phase and that the guinea-pig pituitary when transplanted to a site removed from its normal anatomic position loses its cyclic character. This failure, in all probability, is due primarily to the severance and nonregeneration of its normal neural and vascular connections.

JACOBSEN, Buffalo.

EFFECT OF ANTERIOR PITUITARY-LIKE HORMONE ON THE BLOOD PICTURE IN RABBITS. D. WILSON, Endocrinology **21**:96 (Jan.) 1937.

Clinical evidence indicates that hematopoiesis and discharge of young cells into the circulating blood are controlled by agents in the circulating blood. It has been found that thyroid hormone stimulates the production of red blood cells and lymphocytes and depresses the output of granulocytes; the adrenal hormone stimulates the production of granulocytes and probably also of red blood cells, while the basophil cells of the anterior lobe of the pituitary stimulate all types of circulating cells.

In the study reported here it was found that injections of the gonadotropic hormone from the urine of pregnant women caused marked leukocytosis in normal female rabbits within from five to eight hours. The red cell count remained unaltered. Repeated injections over a long period and at short intervals became ineffectual in producing leukocytosis.

JACOBSEN, Buffalo.

ESTROGENIC ACTIVITIES OF SOME SYNTHETIC PHENANTHRENE COMPOUNDS AND SOME OXIDATION PRODUCTS OF THEELOL. S. A. THAYER, D. W. MACCORQUODALE and E. A. DOISY, J. Pharmacol. & Exper. Therap. **59**:48 (Jan.) 1937.

Three of thirty-two derivatives of phenanthrene were found to cause estrogenic activity in mice. Certain oxidation products of theelol are less active than theelin but more so than the aforementioned phenanthrene compounds. The authors call attention to their previously published statement: "It was found possible to produce full cornification of the vaginal epithelium by smearing alone, without the administration of any estrogenic material."

PILCHER, Cleveland.

PRESENT STATUS OF ENDOCRINOLOGY IN ITS RELATION TO THE CHILD. ROY GRAHAM HOSKINS, Pennsylvania M. J. **40**:167 (Dec.) 1936.

The author states that the child comes under the influence of endocrine factors at the time of his conception and remains vitally under such influence throughout the period of his prepuberal and puberal life. His very generation is dependent on endocrine factors, in that the fertility of both parents is thus conditioned. During the intra-uterine period he is under the influence of the hormones of the mother, and in the later stages, of those of his own glands also. His nourishment during infancy is dependent on the hormone called prolactin, by which the ripened mammary glands of the mother are thrown into activity. Several hormones have important regulatory influences on his growth, both mental and physical.

His maturing at puberty is intimately controlled by his glands. The unfolding of his personality is dependent on hormones which condition both intellectual development and the instinctive drives and emotions on which personality chiefly depends. The relationship of various glands to these several functions is discussed in the light of some of the newer findings.

LOGUE, Williamsport, Pa.

VITAMIN C CONTENT OF THE HYPOPHYSIS. J. GAGYI, Nourrisson **24**:371 (Nov.) 1936.

Lethal doses of diphtheria toxin produce in guinea-pigs hemorrhages and necroses in the adrenals, the corpora lutea and the posterior lobe of the hypophysis. Data have been collected to show that these changes may be due to loss of the vitamin C contained in these organs. In the fatal cases this vitamin disappears from the adrenals and liver several days before it leaves the hypophysis. The young guinea-pig has a greater amount of vitamin C in its pituitary gland than the adult guinea-pig, and the posterior lobe is much richer in vitamin C than the anterior lobe. This is in direct contradiction to the observations of earlier investigators.

McCLELLAND, Cleveland.

ADIPOSITY IN CHILDREN. M. BORNHARDT, Monatschr. f. Kinderh. **67**:270 (Nov.) 1936.

There is a tendency to confuse the adiposity of children developing at puberty with endocrine disturbance such as dystrophia adiposogenitalis. In studying sixty-five cases of juvenile adiposity the writer found only one case belonging to the aforementioned group. She confirms the findings of Rosenstern and Opitz in this respect and urges caution in forming conclusions as to the results of hormone therapy.

GERSTLEY, Chicago.

RELATION BETWEEN THE THYROID GLAND HORMONE AND VITAMIN A. W. FLEISCHMANN and S. KANN, Wien. klin. Wchnschr. **49**:1488 (Dec. 4) 1936.

Continuing along the lines of the research which in recent years has shown a relation between hormones and vitamins, Fleischmann and Kann have confirmed the belief that there is an antagonistic action between the hormone of the thyroid gland and vitamin A.

A series of sturdy mice were divided into two groups. One group was fed with oats and a preparation of vitamin A (A group); the other, with oats and olive oil (B group). Afterward, thyroxin was injected into some animals in each group (A-1 and B-1), while others in each group were used as control animals (A-2 and B-2). Finally, all were given acetonitril (methylcyanide) in amounts which ordinarily would have been fatal. Of the A-2 and B-2 animals, all died. Of sixteen animals in group A-1, three survived (19 per cent); of nineteen animals in group B-1, eighteen survived (84 per cent).

Assuming that the thyroxin gave protection against the acetonitril, this protection was noticeably counteracted by vitamin A.

A further experiment was made with salamanders, some of which were fed olive oil and the others a preparation of vitamin A. In the latter, thyroxin was comparatively ineffective, as shown by slower metamorphosis and less loss of weight than in the olive oil control group, which showed the hyperthyroid symptoms of rapid growth with reduction in weight.

Science has not yet explained the antagonism between vitamins and hormones, but there can be no doubt that it exists. The practical result of these and further experiments will be the possibility of influencing endocrine diseases by diet.

ABT, Chicago.

EFFECT OF HYPERTENSION AND HYPOTENSION OF THE MATERNAL HYPOPHYSIS ON THE GENITAL GLAND OF THE FEMALE FETUS. T. TANIOKA, Jap. J. Obst. & Gynec. **19**:531 (Nov.) 1936.

Stimulation of the hypophysis of the pregnant rabbit by daily injections of anterior pituitary hormone produced a slight increase in the size and weight of the ovaries of the offspring.

Hypofunction of the hypophysis produced by exposure to roentgen rays at ten day intervals during pregnancy produced a slight decrease in the size and weight of the ovaries of the offspring.

ADAIR and POTTER, Chicago.

EFFECT OF FUNCTIONAL ABNORMALITY IN THE MATERNAL PANCREAS ON THE GENITAL GLAND OF THE FEMALE FETUS. T. TANIOKA, Jap. J. Obst. & Gynec. **19**:535 (Nov.) 1936.

The female fetuses born of pregnant rabbits which were treated daily with insulin during the entire period of pregnancy exhibited a slight increase in the size of the ovaries at birth.

In the offspring of rabbits partially depancreatized prior to pregnancy the ovaries showed a slight decrease in size at the time of birth.

ADAIR and POTTER, Chicago.

EFFECT OF FUNCTIONAL DISTURBANCE OF THE MATERNAL ENDOCRINES ON THE GENITAL GLANDS OF THE FEMALE FETUS. T. TANIOKA, Jap. J. Obst. & Gynec. **19**:541 (Nov.) 1936.

In a general review of several papers concerning the effect of maternal hormones on the ovarian development of the fetuses, Tanioka concludes that stimulation of the maternal adrenal cortex, thyroid gland, hypophysis and pancreas causes an increase in the average size of the ovaries of the female offspring.

Decrease in the hormones from these glands causes decrease from normal in the size of the ovaries of the fetuses.

ADAIR and POTTER, Chicago.

THE RESULT OF AN INQUIRY CONCERNING SOME OF THE PROBLEMS OF DIABETES. B. SÖDERLING, Acta pædiat. **19**:217, 1936.

Questionnaires were sent to the chiefs of approximately 100 pediatric teaching institutions in 21 lands, and 31 answers were received from 15 countries. Six questions were asked. The specific questions and a brief summary of the answers which were received follow:

1. "Have you ever observed complete cure with recovery of normal carbohydrate tolerance in a case proved to be one of juvenile diabetes?" Only 3 affirmative answers were received; in one case the correctness of the diagnosis of diabetes appeared debatable.

2. "Approximately how many cases of juvenile diabetes in patients up to 15 years of age have you treated since the introduction of insulin?" The number of cases returned totaled about 1,600. The number of patients treated by the individual clinician varied from 4 (Hirai, Nagasaki; population, 200,000) to 250 (Boyd, Toronto; population, 630,000). The largest numbers were reported by clinicians in English-speaking countries.

3. "How many of these patients have been treated without insulin? How many could be treated for more than two years without insulin?" Of the 1,600 patients, only about 30 could be treated for more than two years without insulin.

4. "Are you of the opinion that all diabetic children should be treated with insulin from the time the diagnosis is made?" Opinions were about equally divided. Many clinicians appeared to fear that the early use of insulin might be conducive to the formation of an insulin habit; others dispensed with insulin for as long as possible in order to spare the children the distress of repeated injections.

5. "What dietetic plans do you follow in the treatment of juvenile diabetes?" The answers can be summarized by stating that there has been little change in the dietetic management of juvenile diabetes in the last few years except a slight relaxation of the rigid regulation of the intake of food; more attention has been paid to the prevention of acidosis and to fostering the nutrition of the child.

6. "Do you attempt to maintain the urine sugar-free?" The answers to this question are about equally divided.

Söderling comments on the answers to the questionnaire and voices an earnest plea for the experimental use of "free diet." McCune, New York.

Relation Between Anterior Pituitary Insufficiency and Function of Stomach and Bone Marrow. I. Snapper, Nederl. tijdschr. v. geneesk. **81:** 265 (Jan. 23) 1937.

In five adults with signs of insufficiency of the anterior lobe of the hypophysis complete gastric achylia was found. In one patient this led to a clearcut pernicious anemia; in one, to a severe hyperchromic blood picture, and in three, to more or less distinct symptoms of combined systemic disease of the spinal cord. In the last patients no abnormalities of the blood were found. Thus a connection can be accepted between insufficiency of the anterior lobe and gastric achylia, a condition which may cause deviations in the blood or in the spinal cord.

van Creveld, Amsterdam, Netherlands.

## Diseases of Muscles, Bones, Joints and Lymph Glands

Experiments with Quinine and Prostigmin in Treatment of Myotonia and Myasthenia. F. Kennedy and A. Wolf, Arch. Neurol. & Psychiat. **37:**68 (Jan.) 1937.

Quinine is as effective in myotonia as prostigmin is in myasthenia. It is established that the action of the two drugs of opposite incidence relieves the two disorders, which are equally opposed. Myasthenia and myotonia are primary disorders of muscle or of the myoneural junction. Beverly, Chicago.

Osteomyelitis of the Sphenoid Bone: Report of Two Cases. L. J. Lawson, Arch. Otolaryng. **25:**1 (Jan.) 1937.

Osteomyelitis of the sphenoid occasionally occurs, though this bone has unique reparative and specific protective properties against invasion. Lawson gives the symptoms of suppuration, outlines the transition to diffuse osteomyelitic infection and notes the complications. He reviews reports of cases found in literature concerning this condition. He then reports two cases, in the first of which osteomyelitis of the sphenoid bone was produced by extension from petrositis and in the second, by reactivation of chronic infection of the sphenoid bone. The findings in each instance are reviewed, the developments cited and the methods of surgical intervention, as well as the medical therapy employed, discussed.

The pathologic examination in the first case revealed typical basilar meningitis. The necropsy in the second case showed that the process had taken the unusual outlet of posterior cervical thrombophlebitis. Lawson states that osteomyelitis of the sphenoid bone requires extensive surgical removal of bone beyond the infected thrombosed blood vessels, a procedure which as yet is not feasible surgically. Greenwood, Chicago.

Differential Diagnosis of Acute Osteomyelitis in Children. J. R. Dolce, Arch. Pediat. **54:** 67 (Feb.) 1937.

Dolce points out several diseases with which a physician might confuse acute osteomyelitis: scurvy, acute appendicitis, cellulitis, acute otitis media and acute rheumatic fever. Orr, Buffalo.

BONE ABSCESS SIMULATING A CYST. D. SLOANE and M. KLIGER, Arch. Pediat. **54**: 77 (Feb.) 1937.

Five weeks prior to admission to the hospital a 10 year old boy injured his right knee. Following the injury he limped and complained of pain in the right hip. Roentgen examination of the right hip showed a rarefied area in the neck of the femur. At the time of operation a large cavity was found in the femur, at the side of the neck. A culture of bone scrapings was positive for Staphylococcus aureus. The patient made a complete recovery.

ORR, Buffalo.

INFANTILISM WITH BONY CHANGES RESEMBLING RICKETS AND CALCIFICATION IN KIDNEYS. C. ASHER, Arch. Dis. Childhood **11**:311 (Dec.) 1936.

Infantilism with renal calcification and bony changes resembling rickets, which failed to heal completely under antirachitic treatment, is described. The biochemical investigations are recorded. It is shown that the condition cannot be explained by vitamin D deficiency, disordered renal function, celiac disease, acidosis or parathyroid hyperplasia alone. Parathyroid hyperplasia secondary to unhealed rickets, persisting after the exhibition of vitamin D, is suggested as a possible cause.

KELLY, Milwaukee.

VACCINE THERAPY FOR OSTEOMYELITIS (RESORPTION OF A SEQUESTRUM). A. CHAKIR and MUNIR, Rev. d'orthop. **24**:60 (Jan.) 1937.

Chakir and Munir report two cases of resorption of a sequestrum in osteomyelitis with use of a vaccine. They used a stock vaccine, propidon, with good results.

RYAN, Vancouver, B. C.

CONGENITAL DISLOCATION OF THE HIP: A NEW TRANSPORTABLE CHAIR FOR USE IN TREATMENT. P. BERTRAND, Rev. d'orthop. **24**:68 (Jan.) 1937.

Bertrand describes a chair which he has devised, permitting ambulant treatment of the child with a congenital dislocation of the hip while in a plaster spica. This chair, made of metal with a leather cushion, is set on casters, and the child is held in a sitting position by a band around the abdomen, fastened to the chair back. The height may be adjusted to the size of the patient so that some locomotion may be attempted by him. The chair may be mounted on an accessory frame of table height if desired. The light weight of the chair permits easy transportation in an automobile or other vehicle.

RYAN, Vancouver, B. C.

PERIOSTEAL DYSPLASIA. F. PARADISO, Lattante **7**:583 (Dec.) 1936.

Paradiso reports the first case of periosteal dysplasia—osteogenesis imperfecta—to be encountered in the pediatric clinic at Catania in its twenty-seven years' existence. The patient—a boy—had been followed for one year. There were twelve fractures at birth and many later; the formation of callus about the fractures was rapid. The child had blue scleras, a normal amount of calcium in the blood, slight hydrocephalus and some signs of hypothyroidism.

HIGGINS, Boston.

THE TEST OF DONAGGIO AND MUSCULAR ACTIVITY IN THE CHILD. P. LUCIANI, Riv. di clin. pediat. **35**:22 (Jan.) 1937.

The test of Donaggio depends on the capacity of the urine to prevent the precipitation of thionine by ammonium molybdate. Thionine is negligible in the urine of normal children but is increased in the urine of patients with muscular dystrophy and frequently in the urine of normal children after exercise.

Luciani made observations on seventy-two children from 6 to 10 years of age who ran a distance of from 300 to 500 meters in between ninety and one hundred

and eighty seconds. In thirty of the children after this exercise Donaggio's test was positive. These children came for the most part from families in poor or moderate economic circumstances. Many of these children showed an exudative or a lymphatic constitution. The conclusion is drawn that the test of Donaggio should be a good means of evaluating the aptitude of a child for physical work.

HIGGINS, Boston.

ETIOLOGY OF A CASE OF TORTICOLLIS. A. DE REZENDE, J. de pediat., Rio de Janeiro **3**:445 (Oct.) 1936.

This torticollis in a 9 year old child was caused by Pott's disease of the cervical vertebrae. The source was pulmonary tuberculosis. The treatment consisted in physical therapy for the tuberculosis and application of a suitable cast for the wryneck. The results were excellent.

SANFORD, Chicago.

SUBACUTE AND CHRONIC NONTUBERCULOUS DISEASES OF THE KNEE JOINT IN CHILDHOOD. H. G. HUBER, Kinderärztl. Praxis **7**:491 (Nov.) 1936.

This is a report and discussion of seven cases in which differentiation of the nontuberculous disease from tuberculosis of the knee joint proved to be very difficult. The final diagnosis was that it was either arthritis (and osteomyelitis), due to mild septicemia, or syphilis.

HEYMANN, Cleveland.

INFLUENCING CREATINURIA IN PROGRESSIVE MUSCULAR DYSTROPHY. A. O. SCHALLY and A. SPITZ, Med. Klin. **33**:90 (Jan. 15) 1937.

A 24 year old woman with typical muscular dystrophy, who had been treated with large doses of amino-acetic acid over a period of several months before being admitted to the clinic, was under observation for three and one half months. Almost daily determinations of urinary creatine and creatinine were made. The excretion of these substances was very irregular, regardless of the diet. Amino-acetic acid was administered for twelve successive days in daily doses of 10 to 20 Gm., and for eleven successive days in daily doses of 20 Gm., without influence on the creatinuria. Insulin and sugar, as well as gympatol (p-methylamino-ethanolphenol tartrate) and extract of adrenal cortex, were also without effect. The case is reported as evidence that the optimism regarding amino-acetic acid therapy expressed in the literature is not justified in all cases.

SIEMSEN, Chicago.

CONGENITAL SYNOSTEOSIS OF THE SEMILUNAR AND TRIQUETRAL BONES. J. REISS, Röntgenpraxis **8**:716 (Oct.) 1936.

Although many mammals exhibit a tendency to simplify the structure of the carpus by reduction of the number of separate bones that it contains, congenital synosteosis of the carpal bones is exceedingly rare in man. An illustrative case is reported.

MCCUNE, New York.

LOCALIZED TRANSVERSE SHADOWS IN THE METAPHYSES OF LONG BONES. N. R. BRAUN, Röntgenpraxis **8**:746 (Nov.) 1936.

A variety of constitutional diseases are capable of producing transverse lines in the metaphyses of the long bones of children, as seen by x-ray projection. Usually in the same patients the lines occur in all of the rapidly growing portions of the skeleton; in other words, they are generalized. Only two previous studies have been published concerning those lines which are occasionally found in a single bone without lines being present in the rest of the skeleton. In 1924 Asada reported on a group of patients who had localized transverse lines; these appeared to be caused by disturbances which involved only one extremity, such as clubfoot

and tuberculosis of the joints. Asada produced similar lines experimentally by causing retardation of growth of a single extremity. In 1930 Gottesleben ascribed the phenomenon to the combined effects of constitutional and local causes.

The case which is reported is that of a 21 year old woman who had had rickets in infancy, a fracture of the right tibia at 12 years and a myxosarcoma developing in the right knee one year before she came under observation. Roentgen examination revealed dense transverse lines near the proximal metaphyses of the right tibia and fibula; similar lines were not present elsewhere in the skeleton. A brief bibliography is given.

McCune, New York.

Sacrococcygeal Tumor. M. Yuba, J. Orient. Med. **25**:809 (Oct.) 1936.

Yuba reports three cases of sacrococcygeal tumor (Middeldorpf) in Manchurian infants of 6 months, 5 months and 3 years, respectively. Each tumor was surgically removed, with permanent recovery. The tumor mass in the first child was a unilocular cyst with a diverticulum; that in the second was a solid teratoid tumor with partial cystic formations, and that in the third was a solid round cell sarcoma. The cyst in the first case was lined with cylindric epithelium, producing melanin. The wall consisted of neuroglial tissue, indicating a probable origin from embryonal medullary rests. The first tumor was a pure malformation, the second a genuine neoplasm as teratoid tumor, and the third a sarcomatous variant of a benign tumor.

Kato, Chicago.

## Diseases of the Eye

Trachomatous Keratitis: A Biomicroscopic Study of Two Hundred and Eighty Indian School Children. P. Thygeson, Arch. Ophth. **17**:18 (Jan.) 1937.

There being some divergence of opinion as to the frequency of pannus among trachomatous Indian children, 248 children ranging in age from 6 to 19 years were examined with the slit lamp. Trachomatous pannus was observed in all but 8 of the 212 children who had trachoma and in 16 of the 36 whose condition was classed as "doubtful trachoma." These observations indicate that pannus occurs early in the course of trachoma, and that slit lamp examination of the limbus and cornea is of value in differentiating this disease from other corneal lesions.

Wescott, Chicago.

Growth in Mass and Volume of the Human Lens in Postnatal Life. R. E. Scammon and M. B. Hesdorffer, Arch. Ophth. **17**:104 (Jan.) 1937.

The lens has a mean weight of almost 66 mg. at birth, which increases about one-half in the first six months, doubles at the end of the first year and increases twofold in the first decade. At 35 years of age the weight of the lens is approximately three times the weight at birth, and at 75 years it approaches four times the weight at birth.

The volume of the lens increases at a rate proportional to age. The absolute and relative increase in specific gravity is much more rapid in the earlier years than in the later years. Most parts of the nervous system make a greater relative gain in the first three years of life than does the lens.

Wescott, Chicago.

Familial Hyaline Dystrophy in the Fundus Oculi or Doyne's Family Honeycomb "Choroiditis." M. Tree, Brit. J. Ophth. **21**:65 (Feb.) 1937.

Tree points out the fact that many pathologic processes of diverse origin in the macular region produce an ophthalmologic picture of whitish spots in the fundus and that a particular degeneration, namely, hyaline change, may be the end-result of different diseases. To Doyne is credited the first definite differentia-

tion of a familial type of "central choroiditis" as a distinct clinical entity. A brief description of Doyne's observations and Collins' histologic report on one of the eyes in Doyne's cases is given. The author reports on seven patients with Doyne's disease whom he has examined repeatedly, giving the refraction, the visual field, the light sense, the threshold for color, the appearance of the fundus and media and the results of physical examination. Among conditions that have sometimes given rise to confusion in diagnosis and which Tree describes are Tay's nonfamilial type of choroiditis, retinitis circinata, cerebromacular degeneration, retinitis punctata albescens, early mild disseminated choroiditis, arteriosclerotic retinitis, renal choroiditis and exudative choroiditis.

The article is illustrated. ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

INFANTILE AND CONGENITAL RETINAL FOLD. A. TILLEMA, Brit. J. Ophth. **21**:94 (Feb.) 1937.

A slight divergent squint had developed in a child 3½ years old, and the eye looked strange. The lens was turbid in its deeper layers, especially at the center. Behind the lens, temporally and below, a fairly well defined mass was seen against the retina. The eye was removed. Microscopic examination showed a few posterior synechiae. The lens was liquefied and vacuolated in the anterior cortex. Delicate fibers of connective tissue were attached to the posterior surface and ran toward the ora serrata. The retina was completely detached. It showed two folds, one extending from the optic papilla toward the pars plana of the ciliary body, downward and slightly outward, and a second just behind the ora serrata, extending in a circular direction. The crests of both folds were attached to strands of connective tissue. All these fibers joined behind the lens in a fairly vascular mass of connective tissue. The optic papilla was 2 mm. in front of the retina. Many of the retinal rods and cones were missing. Many small spaces were filled with a homogeneous coagulation. Scattered leukocytes were present. The retinal veins were surrounded by closely packed lymphocytes. Close to the large fold the retina exhibited disorganization and a hole. In this region the inflammatory changes were most marked. The optic nerve traversed the subretinal space for a distance of 2 mm. From the optic nerve a strong fibrous band continued forward. It contained many fibroblasts. The retina and connective tissue membrane contained scattered polymorphonuclear leukocytes. The central artery of the retina divided into several branches close to the optic papilla. No remnants of a hyaloid vessel were observed.

The inflammatory changes were confined almost entirely to the retina and vitreous, and for this reason it is not difficult to reconstruct the pathologic process. Retinitis, probably metastatic, was followed by abscess formation in the vitreous. This abscess subsided and was organized. Fibrous tissue then contracted and pulled every structure to which it was attached toward the center of the eyeball. Thus the retina, optic nerve and choroid were displaced.

Tillema concludes that in his case the anomaly was caused by inflammation, probably retinitis; in Weve's eighth case it was probably caused by cyclitis of the pars plana of the ciliary body. It is suggested that in Weve's first, fourth, sixth and seventh cases the condition was related to high myopia. For all other cases an inhibition of normal development of unknown origin must be accepted; for the group a familial occurrence has not been accepted.

The article is illustrated. ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

THE MODERN TREATMENT OF SQUINT AND THE PREVENTION OF BLINDNESS. J. B. HAMILTON, M. J. Australia **2**:815 (Dec. 12) 1936.

Hamilton asserts that the treatment of squint should be primarily for the saving of sight and only secondarily for cosmetic reasons. If the amblyopic, squinting eye of a child under 6 years of age is made to work by occlusion of the fixing eye the vision will return rapidly. After recovery from amblyopia, orthoptic exercises are the ideal treatment. They are a slow and time-expending

method and often for lack of time must be supplemented by operation. Cures obtained by orthoptic treatment are permanent, both visually and cosmetically.

GONCE, Madison, Wis.

EMBRYONAL, FETAL, ZONULAR AND CENTRAL CATARACT. G. TAVALORO, Ann. di ottal. e clin. ocul. **64**:721 (Nov.) 1936.

The older literature concerning congenital central (nuclear) cataract is reviewed, as well as that based on modern findings with the slit lamp. A case of bilateral embryonal nuclear cataract is described. The opacity was from 3 to 4 mm. in diameter and corresponded to the size of the lens in the fifth fetal month. In a second case each lens showed three zones of opacity: a central opacity, the most dense, corresponding to the embryonal nucleus; a more peripheral grayish zone with a sharply outlined border, corresponding to the fetal nucleus, and six spokes of opacity radiating from this zone to the periphery of the lens. Signs of defective development and of rickets were present. In a third case only the fetal nucleus was involved, but three layers could be distinguished. The most central was very dense, triangular and corresponded in size only to the region of the anterior Y suture. The second and third were less dense and of a powdery appearance, corresponding to the middle and late periods of fetal life. In a fourth case one eye presented a total cataract, but with a denser central opacity corresponding to the embryonal nucleus, while in the other eye only the fetal nucleus was involved. From these observations and others in the literature Tavaloro would distinguish between the zonular form of cataract in which all the zones of opacity are confined to the fetal nucleus and the more usual zonular, or perinuclear, cataract. The greater density of the most central portion in his nuclear cataract indicates an origin of the opacity very early in fetal life and in the most central part of the lens, in contradistinction from perinuclear zonular cataract, which begins in postnatal life or late in fetal life. It is also possible to distinguish, according to the size of the opacity, between embryonal cataract, which develops during the first four months of intra-uterine life, and fetal cataract, which develops later in fetal life. If opacification continues until the end of fetal life, a total cataract will result.

S. R. GIFFORD, Chicago. [ARCH. OPHTH.]

OPHTHALMIC HERPES ZOSTER. M. DE ALENCAR, F. DE TOLEDO and I. MENDES, Arch. de pediat., Rio de Janeiro **9**:131 (Feb.) 1937.

The authors describe this condition in a 9 year old boy. Excellent photographs and drawings of the nerve supply to the region of the eye are given.

SANFORD, Chicago.

HEREDITY OF HYALINE BODIES OF THE DISK. M. LEIMGRUBER, Arch. f. Ophth. **136**:364 (Dec.) 1936.

To the five known families in which several members of one or two successive generations showed hyaline bodies (drusen) of the disks Leimgruber adds five more. None of the patients revealed signs of active or healed neuritis. Some brothers or sisters of patients with definite hyaline bodies showed slightly elevated, indistinctly outlined "pseudoneuritic" disks. For these, the presence of deeply situated and therefore invisible hyaline bodies is assumed. "Hyaline bodies may be the result of neuritis or the result of an inherited tendency toward the deposition of hyalin."

P. C. KRONFELD, Peiping, China. [ARCH. OPHTH.]

PSEUDO-ATROPHY OF THE OPTIC NERVE IN YOUNG INFANTS. K. T. A. HALBERTSMA, Nederl. tijdschr. v. geneesk. **81**:1230, 1937.

Halbertsma reports the clinical history of a girl 8 weeks old who was brought to him by the parents with the complaint that the eyes had a peculiar staring expression which had made them fear that the child might be blind. The ophthal-

mologic examination revealed an abnormal behavior of the pupils and a peculiar coloration of the optic papillae. On the basis of another examination made three weeks later, the disorder was diagnosed as pseudo-atrophy of the optic papilla probably resulting from retarded myelinization of the pupillomotor fibers of the optic nerve. Several successive examinations disclosed gradual improvement in that the pupillary reactions became more normal and the peculiar coloration of the papillae began to disappear. The author points out that the condition in this case corresponds to that described as pseudo-atrophy of the optic nerve in the new-born by Beauvieux in 1926. He also cites the signs which, according to Beauvieux, differentiate pseudo-atrophy of the optic nerve from true congenital atrophy of the optic nerve.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

## Skin Diseases; Allergy

ECZEMA IN INFANCY AND CHILDHOOD: THEORETICAL CONSIDERATIONS AND SOME CONTRIBUTING FACTORS. H. GOODMAN and M. BURR, Arch. Pediat. **54**:30 (Jan.) 1937.

Goodman and Burr have analyzed the records on 206 cases of eczema in infants. The incidence was 105 in males and 101 in females. Forty-six per cent of the infants showed evidence of the disease within the first month of life, and 80 per cent, within the first three months. Extreme changes in temperature aggravated the condition. Constipation was present in varying degrees in 85 per cent of the patients.

ORR, Buffalo.

RACIAL INCIDENCE OF ACRODYNIA. J. ZAHORSKY, Arch. Pediat. **54**:56 (Jan.) 1937.

Zahorsky observed the interesting fact that, of sixty children with acrodynia, fifty-one were of German, two of Slovak, one of Polish, two of French, one of Irish and three of Scotch extraction. The ancestries of several patients were traced to southwestern Germany, where the disease is reported to be most prevalent.

ORR, Buffalo.

MEDICAL TREATMENT OF RINGWORM OF THE SCALP. D. E. H. CLEVELAND, Canad. M. A. J. **36**:38 (Jan.) 1937.

In thirty-one cases, ringworm of the scalp, presumably due to the human type of Microsporon, was treated by the Lieberthal method, with only one failure. The time required for cure (a negative finding under the Wood light being the accepted criterion of cure) ranged from three to twenty-two weeks. The method consists in clipping the hair short and keeping it clipped close throughout the treatment, shampooing the scalp each morning with soap and water, and rubbing in 10 per cent ammoniated mercury ointment nightly and on alternate mornings. On the intervening mornings, all visible patches were painted with 5 per cent aqueous solution of mercurochrome-220.

The author stresses the importance of examining the scalp with the Wood light to determine the presence of any fluorescent hairs so that these may be treated to prevent recurrence.

MOORE, Omaha.

SPECIFIC THERAPY IN RHUS DERMATITIS. H. SHARLIT and B. A. NEWMAN, New York State J. Med. **37**:61 (Jan. 1) 1937.

Standard rhus extracts are generally useless or undependable. An effective extract has been prepared as follows: Freshly gathered ivy leaves were thoroughly dried at a temperature of 50 C. These dried leaves were broken up in a sieve with a coarse mesh, thus sifting out for elimination bits of twig and midrib. Then 10 Gm. of leaves was extracted with 100 cc. of absolute alcohol for seventy-two hours at room temperature and filtered. This filtrate was kept as a stock solution.

One-tenth cubic centimeter of a 1 : 1,000 dilution of the stock solution was given hypodermically on three successive days with but little local reaction. Sixty-three of seventy-four patients received complete relief in four days. Patch tests were made on all of the patients to prove the diagnosis.

AIKMAN, Rochester, N. Y.

LITTLE RECOGNIZED TYPES OF ALLERGY. T. W. CLARKE, New York State J. Med. **37**:236 (Feb. 1) 1937.

By a review of the literature and a brief report of cases Clarke shows how many symptoms and disease conditions may be due to allergy.

AIKMAN, Rochester, N. Y.

ANAPHYLAXIS FROM BANANAS. G. BRIGUGLIO, Riv. di clin. pediat. **34**:1055 (Nov.) 1936.

A boy of 15 months had a family history of asthma on the mother's side. He had been breast fed for seven months and then given a diet of cow's milk and cereal up to ten months. At that time he showed some signs of indigestion, because of which milk was withdrawn from the diet. Bananas were given and were assimilated quite satisfactorily. Two months after the treatment with bananas had been discontinued, the child was again given bananas; following the ingestion of the fruit he presented a serious allergic reaction, with vomiting, profuse watery diarrhea—the stools also containing blood and mucus—and marked urticaria which lasted twelve hours. The child recovered completely, but twenty days later, following the eating of another banana, vomiting, diarrhea, cold sweats and cardiovascular depression ensued; there was no urticaria.

HIGGINS, Boston.

MENINGEAL REACTIONS IN ERYTHEMA NODOSUM. D. DENES VON MÓRITZ, Monatschr. f. Kinderh. **67**:255 (Nov.) 1936.

Von Móritz reports ten cases of erythema nodosum accompanied by meningeal reactions. Lumbar puncture showed these to be divided into three types: (1) characterized by increased intracranial pressure, with large amounts of cerebrospinal fluid containing a reduced quantity of protein; (2) characterized by a perfectly normal spinal fluid, but under increased pressure; (3) characterized by spinal fluid showing an increased amount of protein and cells.

GERSTLEY, Chicago.

SWEAT SECRETION OF CHILDREN. J. ADACHI, J. Orient. Med. (Abstr. Sect.) **25**:95 (Dec.) 1936.

Adachi conducted the following experimental observations in nine children ranging in age from 11 months to 6 years.

EXPERIMENT 1.—Regional variations in the amount of perspiration: Twenty-two representative portions of the body surface were covered with small pieces of blotting paper, about 4 by 4 cm. in size, each piece being covered with a corresponding celluloid dish in order to prevent evaporation. The experimental subjects were placed in a warm room for ten minutes, and the weight of the paper before and after the experiment was determined in each case. In another series of experiments the amount of perspiration was determined by the discoloration method of Minor, the degree and intensity of staining being the index of secretion.

According to results of these experiments, the forehead perspires most profusely, next in order being the anterior and posterior surfaces of the trunk; the amount of perspiration on the lateral surfaces and the extremities is remarkably low. The upper extremities perspire more than the lower, and on the former, perspira-

tion increases peripherally, while in the latter this relationship is reversed. These observations agree with those recorded by Ikeuchi and Kuno in adults.

EXPERIMENT 2.—Quantity of perspiration: The difference in the body weight before and after ten minutes' stay in a hot chamber was measured by means of the Sauter balance. The amounts of perspiration, calculated per square meter of body surface, were compared in children and adults. The results showed no consistent difference between children and adults.

EXPERIMENT 3.—Active sweat glands: The number of active sweat glands per sixteen hundredths of a square centimeter of the skin was determined by Jürgensen's method on different regions of the body in three children during the period of their most profuse sweating. The glands were found to be most numerous on the forehead, somewhat less numerous on the dorsum of the hand and least numerous on other portions of the extremities, so that the ratio of the number of sweat glands on the forehead to that on the extremities was 2:1. The regional relationship of the amount of perspiration seemed to correspond approximately to that of the density of sweat glands.

The anatomic observations revealed the number of active sweat glands per unit of skin area to be much greater in children than in adults, and their density to be greatest in the extremities in children and least in the extremities in adults. These observations led to the conclusion that the amount of perspiration depends primarily on the number of actively functioning sweat glands. Since children are born with a full quota of sweat glands, the density of the glands becomes less and less as the skin surface expands with growth. Not all sweat glands are in active function, but they may be activated according to the physiologic stimulus to meet the needs of any given situation for the maintenance of normal health.

KATO, Chicago.

PROBLEM OF HERPES ZOSTER. S. A. GLAUBERSOHN and S. E. TRACHTENBERG, Acta pædiat. **19**:209, 1936.

Two cases are reported. In the first, exposure of a susceptible person to chickenpox led to an attack of herpes zoster; in the second, exposure to zoster produced varicella.

The etiologic connection between herpes zoster and varicella was first suggested by Bokay, of Budapest, in 1888; in 1928 Bokay was able to collect 200 cases which illustrated this relationship; some of these he collected from the literature, and some were part of his personal experience. Despite the large number of clinical and experimental observations, the fundamental biologic relations between herpes zoster and varicella remain unsolved.

This paper contains an extensive discussion of the conflicting clinical and experimental observations relating to the perennial controversy. The opinion is expressed that a conclusive answer will not be obtained until the cause or respective causes of the two infections are identified and studied experimentally. Glaubersohn has recently had some success in preserving the virus of herpes zoster in tissue cultures. This opens the way for further investigation of the virus and for the possible use of tissue cultures in the preparation of antigens for complement fixation tests; up to the present time the use of such cultures has not been satisfactory.

MCCUNE, New York.

A SIMPLE TREATMENT OF ANGIOMA. E. VAN MINDEN, Nederl. tijdschr. v. geneesk. **79**:5642 (Dec. 7) 1935.

Van Minden was able to obtain the disappearance of angioma in eight of nine young children by vaccinating them against smallpox around the places where the angioma existed (arms, legs and trunk); those on the heads of the children he treated in the usual way by irradiation.

VAN CREVELD, Amsterdam, Netherlands.

A Family with Erythrokeratodermia Variavilis. E. H. Hermans and C. P. Schokking, Nederl. tijdschr. v. geneesk. **80**:5120 (Nov. 14) 1936.

This is a description of a family in which the father, five daughters and one son were suffering from this disease, all to different degrees.

S. van Creveld, Amsterdam, Netherlands.

Two Rare Localizations of the Botryomycoma. L. I. Swaab, Nederl. tijdschr. v. geneesk. **80**:5123 (Nov. 14) 1936.

This is a description of two cases of a rare localization of granuloma telangiectaticum, one in a girl aged 6, in whom a small tumor of the mucous membrane of the urethra was found, the other in a girl of 11 years, in whom there appeared to be a small tumor of the perineum, near the anus. In both cases the only complaint was of loss of blood, which had been regarded as precocious menstruation.

van Creveld, Amsterdam, Netherlands.

Dermatitis Bullosa Caused by Petroleum. C. H. Beek, Nederl. tijschr. v. geneesk. **81**:472 (Jan. 30) 1937.

A boy of 3 years showed dermatitis bullosa on those areas of skin which had been in close contact with his clothes when these were accidentally soaked with petroleum. The dermatitis closely resembled a combustion of the second degree. Beek is of the opinion that such dermatitis appears only when there exists acquired or congenital sensitivity to petroleum. van Creveld, Amsterdam, Netherlands.

## Surgery and Orthopedics

Fracture of the Femur in Children. G. M. Dorrance, Ann. Surg. **105**:584 (April) 1937.

The fact that the prognosis for uncomplicated fracture of the femur in a child is excellent probably accounts for the variety of treatments recommended.

The most important consideration in any fractures of a child's bone is that the growth of the bone is still active. Following such a fracture there is rapid deposition and ossification of callus, followed by equally prompt absorption of any excess of callus and rectification of deformity, usually leading to a result without deformity. In addition to this remodeling at the site of fracture, there occurs overgrowth of bone in the longitudinal direction, which often compensates for any shortening. Shortening up to ½ inch (about 1 cm.) need cause no grave concern. Correct alinement is unquestionably the most important requirement for good results.

The author quotes Kellogg Speed as stating that in children between the ages of 2 and 4 years callus is normally formed in two weeks and that in children under 12 years of age callus is fully formed within three or four weeks.

The author describes his method of treating a fracture of this type. He places extension on both legs and thighs by means of adhesive plaster and elevates the foot of the bed to a height where the bed stands approximately at an angle of 45 degrees with the floor. This method may be used in children up to 12 years of age.

Bantin, Omaha.

Congenital Dislocation of the Hip. G. W. Van Gorder, New England J. Med. **215**:613 (Oct. 1)) 1936.

There were fifty-eight patients in all, with seventy-three dislocated hips. In only forty-six of the patients, comprising fifty-five dislocated hips, could the treatment be followed to the end-results. The ages of the patients were as follows: under 6 years of age, 16; from 6 to 15 years, 18; from 15 to 30 years, 11, and over 30 years, 2.

Of the fifty-five dislocated hips with end-results, sixteen were treated by closed reduction, fifteen by open reduction, eight by open reduction plus a shelf, and sixteen by shelf operation alone. Good functional results were obtained in 88 per cent of the closed reductions, in 27 per cent of the open reductions, in 25 per cent of the "open reductions plus shelves" and in 50 per cent of the cases having shelf stabilizations alone.

The author believes gentle closed reduction should be attempted in all children under 3 years of age. If reduction fails, or if the hip is not secure after six months in plaster, open reduction is indicated. In children over 3 years of age, open reduction is advised. In persons over the age of from 9 to 10 years, the shelf stabilization operation alone is indicated.

GENGENBACH, Denver.

REPAIR OF CONTRACTURES RESULTING FROM BURNS. V. H. KAZANJIAN, New England J. Med. **215**:1104 (Dec. 10) 1936.

Emphasis is placed first on prophylactic treatment by controlling infection of the burned areas and preventing formation of contractures. The various methods of skin grafting are described in detail, as are the procedures for the treatment of specified areas, such as eyelids, cheek, nose, mouth, neck, axillae, hands and fingers. The article is well illustrated and gives many case reports.

GENGENBACH, Denver.

ACUTE INTESTINAL OBSTRUCTION FOLLOWING HERNIA INTO ASCENDING MESOCOLON. J. W. CHAMBERLAIN, New England J. Med. **216**:299 (Feb. 18) 1937.

Among the mechanical causes of acute intestinal obstruction, herniation of the bowel through an orifice in the mesentery is one of the least frequently encountered. A case is reported. The patient, an 11 year old boy, complained of generalized abdominal pain and vomiting. The abdominal cavity was entered through a low incision in the right rectus muscle. The appendix and cecum were delivered into the wound without difficulty, and no abnormality was noted. The terminal part of the ileum was picked up. It was collapsed, and about 16 inches (40.5 cm.) proximal to the ileocecal junction it disappeared in a mass just medial to the ascending colon. The mass was seen to be a loop of bowel that had herniated through a small ring in the posterior parietal peritoneum. Both limbs of the loop, however, were collapsed. On further exploration, it appeared that a second loop of bowel had also herniated through the small opening formed by the arching mesentery of the first loop and the posterior abdominal wall. It was more distended than any other loop and was somewhat discolored. Reduction of the herniation of this second loop was accomplished first and without difficulty. On stretching the narrow ring in the posterior parietal peritoneum, the first loop was then easily delivered into the abdominal cavity. The opening was easily closed with a running stitch, the appendix was removed, and the abdominal wall was sutured in layers. The patient had no further pain or vomiting and made an uneventful convalescence.

GENGENBACH, Denver.

TOXIN FORMATION IN BURNED TISSUES. W. C. WILSON, J. S. JEFFREY, A. N. ROXBURGH and C. P. STEWART, Brit. J. Surg. **24**:601 (Jan.) 1937.

Because of recent adverse criticism that acute toxemia of burns is caused by formation of a toxin or toxins in burned tissue, which are absorbed into the circulation, experimental investigations were carried out. Excessive heat was applied to the skin of a rabbit with the result that a considerable quantity of edema fluid accumulated in the subcutaneous tissue. This fluid was collected as aseptically as possible and its toxicity tested by injecting it subcutaneously, intravenously and intraperitoneally into unanesthetized rabbits and intraperitoneally into mice. The following conclusions were reached:

1. Edema fluid which accumulates in a burned area gradually acquires toxic properties. When collected at forty-eight hours after burning, it is frequently lethal to healthy animals of the same species.

2. The development of toxicity is independent of the action of bacteria; there is evidence that autolysis of injured tissue is the responsible mechanism.

3. A study of the action of toxic edema fluid suggests that there is more than one toxic component and that the proportions of the components vary in different samples.

4. The effects produced include toxic action on the nervous system, depression of the circulation and degeneration of liver cells.

5. The toxic principles are associated mainly with the globulin fraction. The evidence indicates that the more active principles are the higher protein derivatives.

6. The relation of these results to the etiology of acute toxemia of burns in man is mentioned. Features which require further investigation are indicated.

SUMMERFELDT, Toronto, Canada.

## Miscellaneous

THE COMPLICATIONS AND HAZARDS OF FEVER THERAPY: ANALYSIS OF ONE THOUSAND CONSECUTIVE FEVER TREATMENTS WITH THE KETTERING HYPERTHERM. R. M. STECHER and W. M. SOLOMON, Ann. Int. Med. **10**:1014 (Jan.) 1937.

The patients selected for treatment included those with acute and chronic arthritis, rheumatic fever, chorea, syphilis and other conditions. The technic used for the production of fever is given. The treatments are classified as mild and severe, depending on the degree and duration of the fever produced.

The complications and hazards of fever therapy depend primarily on the height and duration of the fever. A temperature of 107 F. maintained for five hours or longer proved under proper conditions of supervision to be a practical and satisfactory procedure.

READING, Galveston, Texas.

ARGYRIA. A. W. STILLIANS, Arch. Dermat. & Syph. **35**:67 (Jan.) 1937.

Stillians reviews the literature on argyria. The discoloration may be local or generalized and may be due to silver absorbed during contact with the metal in industry or in therapeutic use of silver preparations, the most common instance being the continued unsupervised use of silver compounds by the laity in self-treatment for nose and throat ailments. The diagnosis is not difficult in that "in no condition is there a bluish discoloration of the parts exposed to light while the rest of the skin remains ashy gray or even nearly normal in color." The only ideal treatment is prophylaxis. Only one case of cure of generalized argyria has been recorded besides this one reported by the author. In his treatment he gave sodium thiosulfate orally and intravenously in large doses for one month, then methenamine intravenously for one month, without definite results. However, a plaque painted to match the skin was made at the onset of the treatment, and by comparison the "result was wholly satisfactory." The skin, because of the action of light, is probably the last to release its silver deposits. Local treatment consists in the intradermal injection of 1 per cent potassium ferrocyanide and 6 per cent sodium thiosulfide. In the case reported, each injection left a light spot almost as pale as normal skin. By many injections of the reducing solution the whole anterior portion of the face was cleared except for the lower eyelids. If argyria develops in a child, and the silver is discontinued at once, the prognosis is fair, for as the child grows, the silver deposit spreads over a larger surface, and in this way the color is lightened.

DULIN, Iowa City.

ACUTE NICOTINE POISONING: REPORT OF A CASE IN A CHILD. H. W. WILLIS, J. Pediat. **10**:65 (Jan.) 1937.

The classic features of nicotine poisoning are sweating, nausea, vomiting, dyspnea, coma, convulsive seizures, pupillary changes, slowing of the pulse rate in the beginning of the attacks and later acceleration, subnormal temperature and absence of tendon reflexes. These symptoms rapidly become more severe, and death follows in the majority of cases. In a few cases the symptoms subside and the patient recovers completely in a few hours. Willis describes nicotine poisoning in a child 5 years of age, to whom an enema of 60 cc. of strong tobacco juice in 1,000 cc. of water had been given for pinworms. After repeated injections of caffeine with sodium benzoate U.S.P. and cleansing enemas, the child made a complete recovery. The literature is reviewed and experiments are quoted in which artificial respiration and injection of epinephrine hydrochloride for circulatory failure have been found of definite value.

RAUH, Cincinnati.

DIAGNOSIS AND TREATMENT OF ACCIDENTAL POISONING IN CHILDREN. J. AIKMAN, New York State J. Med. **36**:1769 (Nov. 15) 1936.

Accidental poisoning in children occurs more frequently than mortality rates indicate. Without a history of ingestion of poison, the diagnosis becomes a serious problem. Poisoning must be suspected in unexplained collapse, unconsciousness, convulsions, cyanosis and even gastro-enteritis. Skin rashes produced by drugs cause confusion. Respiratory symptoms occur from inhalation of zinc stearate and strong acid fumes and in kerosene poisoning. All drugs and poisons should be kept out of reach of small children. Active treatment is discussed, especially the desirability of having outlines for treatment available in dispensaries and emergency departments. The outline prepared by Hanzlik for the San Francisco Department of Health is recommended.

FROM THE AUTHOR'S SUMMARY.

MECHANISM OF VISCERAL PAIN. H. J. WILKINSON, M. J. Australia **1**:48 (Jan. 9) 1937.

Having observed that pain due to any disorder of the viscera is accompanied by a distinct lowering of the temperature of the skin over the seat of pain and that it is relieved by infiltration of the cool area with 2 per cent procaine hydrochloride, Wilkinson believes that the neural mechanism involved in the production of so-called referred pain is a viscerovasomotor reflex. The visceral afferent nerves when adequately stimulated cause reflex vasoconstriction in the somatic peripheral structures, and thus conditions arise here which lead to stimulation of the pain endings and to the production of pain sensations. The pain is thus felt in the somatic tissue not because it is referred here but because the pain nerves here are actually stimulated. The lowering of the temperature of the skin is merely a manifestation of the vasoconstriction and associated phenomena which provide the adequate stimulation for pain impulses, and is not to be regarded as the cause of the pain. Distinctly localized pain, hyperalgesia and protective rigidity are also sometimes due to the same mechanism but can also be due to similar effects produced by stimulation of somatic afferent nerves arising in the sensitive parietal tissues of the body cavities.

GONCE, Madison, Wis.

"KNOPPIE-SPIDER" ANTIVENENE. M. H. FINLAYSON, South African M. J. **10**:735 (Nov. 14) 1936.

Finlayson announces the preparation of an antitoxin (goat) against Latrodectus indistinctus. The antitoxin is to be issued free to physicians of South Africa for the treatment of "knoppie-spider" bite. (Finlayson previously reported that this antitoxin completely neutralizes not only the homologous venom but the venoms of Latrodectus geometricus and Latrodectus concinnus.)

GONCE, Madison, Wis.

PHYSICAL EDUCATION AND HELIOTHERAPY. P. F. ARMAND-DELILLE, Ann. méd.-chir. **1**:53 (Nov.) 1936.

The paper reports the observations of the members of the third International Congress of Fresh Air Schools. The general organization and aims of the primary and secondary schools are presented. It is pointed out that the schools furnish not only the usual didactic instruction but training in agriculture, animal husbandry and botany. Much attention is given to physical education and recreational guidance. Attention to all of these factors results, it is claimed, in children of better mental, physical and moral stature.

DIETRICH, Los Angeles.

DISEASES OF CHILDREN IN 1936. P. LEREBOULLET and F. SAINT GIRONS, Paris méd. **2**:313 (Nov. 7) 1936.

This is a review of the pediatric literature for 1936.

LESLIE, Evanston, Ill.

A HOSPITAL SERVICE TO ENABLE HEALTHY INFANTS TO NURSE THEIR SICK MOTHERS. R. S. CUIZZA, Lattante **7**:592 (Dec.) 1936.

When a nursing mother is admitted to the Maria Vittoria Hospital, Turin, Italy, arrangements are made to admit the baby also, in order that the breast feeding may not be interrupted. Since 1911 hospital care has thus been afforded to 377 healthy nurslings under 3 months of age. Of these, 150 were discharged on breast feedings entirely and 195 partly on breast feedings. Thirty had been weaned. Forty-seven of the infants had been taken from the breast at the time of the mothers' admission to the hospital.

HIGGINS, Boston.

USE OF RHINO-VASOGEN IN PEDIATRIC PRACTICE. M. BARWICH, Med. Klin. **33**: 341 (March 5) 1937.

Very good results were obtained in the treatment of acute and chronic rhinitis in infants and children by the use of an extract of chamomile, menthol and eucalyptol in a preparation of petrolatum. The compound possesses marked penetrating properties yet is nonirritating.

SIEMSEN, Chicago.

HEAT INJURY OF THE NURSLING. E. FLUSSER, Monatschr. f. Kinderh. **67**:288 (Nov.) 1936.

Flusser discusses the different types of reaction of the infant to heat. Finkelstein and also Rietschel showed years ago that children with beginning alimentary intoxication could be greatly benefited by allowing their bodies to cool. Flusser thinks that in many cases the severe reaction of the nursling to overheating is not due entirely to the overheating but is due to a combination of this plus a mild infection. When the body is allowed to cool by removal of excess covering, the temperature may drop 4 or 5 degrees but still remains slightly above normal. Flusser interprets this as being due to the presence of a mild infection. Infants with dermatitis are particularly prone to have high temperatures if covered too warmly. Flusser thinks that psychic influences may at times cause high fever. He describes attacks of temper in children wrapped in featherbeds, in which the temperature rose 2 F.

On the other hand, children in whom the temperature is high through infection such as pneumonia are not likely to be injured by too many covers and are perhaps more harmed than benefited by too few. While he realizes that tepid sponges and Priessnitz compresses have their place, he rather leans to the idea that there is an element of danger in these treatments and that antipyretic treatment is better conducted with medicaments.

GERSTLEY, Chicago.

# Society Transactions

## SOCIETY FOR PEDIATRIC RESEARCH

*Annual Meeting, May 4, 1937*

FRANCIS SCOTT SMYTH, M.D., *President*

A. ASHLEY WEECH, M.D., *Secretary*

### Morning Session

IMMUNOLOGIC RELATIONSHIPS OF TYPE-SPECIFIC POLYSACCHARIDE FROM THE TYPE I MENINGOCOCCUS. DR. H. W. SCHERP, Philadelphia.

The reaction of the type I meningococcus polysaccharide (SI) of Scherp and Rake with both type I and polyvalent antimeningococcus horse serums has been analyzed, using the technic introduced by Heidelberger and Kendall for quantification of the precipitin reaction.

The reaction between SI and homologous monovalent serum followed the course typical of a system containing one haptene and its antibody. Over a wide range, the amount of antibody (as nitrogen) precipitated was related to the amount of SI added by an equation of the type $N = AS - BS$.[2]

The reaction between SI and polyvalent serum fell into two parts. For the first part, the equation was of the form $N = K + AS - BS$,[2] in which K had a value not larger than 0.05 (all values being reduced to the basis of 1 cc. of serum) and probably represented the lipoid nitrogen which Goodner and Horsfall found to be a common nonspecific constituent of antigen-antibody aggregates. For the latter range of the reaction, the equation was of the same form but with entirely different constants. K was large (0.3 to 0.4) and the values of A and B were such that the curve was markedly flat, instead of rising steeply as it did in the first range of the reaction. This was interpreted to indicate the presence of two haptenes and their antibodies. The evidence suggests that SI as prepared contains a large proportion of type-specific polysaccharide, accompanied by a small proportion of group-specific polysaccharide, and that commercial polyvalent antimeningococcus serums contain a small proportion of type-specific antibody, accompanied by a large proportion of group-specific antibody. It was also found that these serums contained nearly as much agar-specific antibody as antimeningococcus antibodies.

DISCUSSION

DR. J. D. TRASK, New Haven, Conn.: Is the shape of the parabola the same for rabbit serum and horse serum?

DR. H. W. SCHERP, Philadelphia: Drs. Heidelberger and Kendall have just published a paper in the *Journal of Experimental Medicine* (**65**:647, 1937) which covers that point. The equation has exactly the same form.

COMPARISON OF THE RESPONSE TO ANTISERUMS IN HUMAN AND IN MOUSE MENINGOCOCCIC INFECTIONS. DR. HATTIE E. ALEXANDER, New York.

The mouse protection test seems to offer a reliable objective method for testing serums at the beginning of an epidemic, for it has been demonstrated in this laboratory that three different serums protect against a number of type one strains to similar degrees.

Using the serum employed therapeutically against the organism isolated from the patient, it was not possible to demonstrate a correlation between the individual

therapeutic response and the protective value in mice. The duration of infection prior to therapy and the age of distribution of the patients were similar in the group in which the disease was fatal and the recovered group. Among the patients whose disease was fatal only those who had received treatment for at least forty-eight hours were included in this study. On the whole the clinical response to these serums in a large series was very good, resulting in as low a mortality as one could expect during an epidemic. Likewise the protection against 20 different strains in mice was excellent. Therefore, the evidence suggests that there is a broad correlation between mouse protection and therapeutic value and that failure of a patient to respond to a serum which gives excellent specific protection in mice must be due to variation in the patient's ability to respond rather than to lack of specificity of the serum.

DISCUSSION

Dr. H. W. Scherp, Philadelphia: I should like to raise the question of the effect of the agar antibody on the mouse protection test. I presume Dr. Alexander's organisms were grown on agar as is customary; Zozaya has shown and my associates and I have obtained results indicating that meningococci grown on agar can be agglutinated by a serum containing the agar antibody. In other words, the organisms become coated with agar antibody, and I wonder—there is no answer for this at the present time, of course—if the fact of coating the organisms grown on agar with the agar antibody present in these various serums might not have some effect on the mouse protection test.

Dr. Hattie E. Alexander, New York: As Dr. Scherp says, there really is no answer to that question on the basis of objective evidence. I suspect that one would have to grow organisms on the agar for a rather long period. I believe it has generally been found to be true that a considerable period is necessary for them to take on the antigenic qualities of the agar. All of these strains were isolated from the original spinal fluid, dried, and then not grown on agar until forty-eight hours before use in the mouse protection test.

Serologic Variation in Strains of Shigella in Relation to Human Infection. Dr. P. Dooley, New York.

Strains of Shigella from 50 children with bacillary dysentery were studied for their agglutinability at the time of their primary isolation and on isolation during subsequent stages in the evolution of the infection. Strains isolated late in the course of the infection may show complete antigenic dissociation when compared with strains isolated from the same patient early in the course. This in vivo dissociation closely follows that which may be observed in laboratory cultures of the original strains. On the basis of agglutinability alone, it seems impossible to classify strains of Shigella.

DISCUSSION

Dr. Hattie E. Alexander, New York: From a purely practical standpoint, I should like to ask whether by combining the types of organisms giving this response to serums one is able to produce an antiserum which is specific against all of the strains isolated from patients.

Dr. J. D. Trask, New Haven, Conn.: If Dr. Dooley uses the methods of classification employed by Bruce White, does he still find the antigenic make-up of the dysentery group as complicated as he has indicated?

Dr. P. Dooley, New York: In answer to Dr. Alexander's question, it is true that it is very easy to prepare a polyvalent diagnostic serum by combining a number of these strains. It is also true that certain ones of these strains will have almost completely polyvalent properties themselves, so that, although a good deal of selection is possible, sometimes not much is necessary. Certain of the commercial polyvalent serums prepared for diagnostic purposes are absolutely effectual in all of the epidemics my co-workers and I have seen.

With regard to the question asked by Dr. Trask, I do not know.

EFFECT OF LYOPHIL POOLED ADULT SERUM ADMINISTERED BY MOUTH ON THE POSITIVE DICK TEST AS COMPARED WITH OTHER METHODS OF ADMINISTRATION. DR. A. C. MCGUINNESS and MR. E. H. HEMPHILL, Philadelphia.

Eighty males whose reactions to the Dick test were positive, ranging in age from 10 to 50 years, with an average age of about 18 years, were divided into four groups, the division being made so that the average intensity of the reactions in each group, as well as the average age of each group, would be approximately the same. The four groups were then treated as follows:

Group I received 30 cc. of pooled adult lyophil serum intramuscularly, dissolved in 12 cc. of sterile distilled water.

Group II received 30 cc. of pooled adult lyophil serum oraliy, the serum being given on an empty stomach diluted in about 4 ounces (118 cc.) of iced alkaline water, as suggested by McKhann in his studies on the oral administration of placental extract.

Group III received 30 cc. of pooled adult serum orally in the form of 12 phenyl salicylate-coated 2.5 cc. tablets.

Group IV, receiving no serum, acted as a control group.

Beginning two days after the administration of serum, all four groups were tested with Dick toxin twice a week for twenty-four days.

In order to decrease the error, all tests were read by the same worker, and all Dick toxin employed for the testing came from one batch specially prepared for the purpose. All serum administered in the study came from one batch of pooled adult serum drawn from 100 donors whose reactions to the Dick toxin had been found to be negative. The test subjects were feebleminded but in good physical health. There was no scarlet fever in the institution at the time the work was carried out.

While there was a decided difference in the average readings of the reactions in the four groups, the fact that there was a certain amount of variation in the reactions observed in the untreated controls was somewhat disturbing. The average readings in the control group remain fairly constant. Several suggestions are offered for the individual variations, the most probable of which are (1) slight inaccuracies in the dosage of toxin, (2) inaccuracy in interpretation of the intensity of erythema and (3) placing tests on areas of skin which may have been slightly desensitized by previous tests.

An analysis of the results obtained suggests:

1. Oral administration of serum in liquid form in iced alkaline water and administration of serum in the form of phenyl salicylate-coated tablets were about 75 per cent as effective as intramuscular injection of serum in producing an immediate (in two days) drop in skin sensitivity.

2. Oral administration of serum in liquid form in iced alkaline water was about 45 per cent as effective as intramuscular injection of serum in maintaining diminution in skin sensitivity after the initial drop.

3. Oral administration of serum in the form of tablets coated with phenyl salicylate was about 67 per cent as effective as intramuscular injection of serum in maintaining diminution in skin sensitivity after the initial drop.

DISCUSSION

DR. W. L. BRADFORD, Rochester, N. Y.: I should like to ask Dr. McGuinness if he has tried the reaction of this serum on the heat-labile and heat-stabile components of the Dick toxin. By observing the effect on these fractions separately, the effect on the real toxic and the allergic components of the material would no doubt be brought out more clearly.

DR. V. W. LIPPARD, New York: I should like to ask Dr. McGuinness whether he did all of the tests on approximately the same cutaneous areas. If so, a refractory period after the first intense reaction might be expected.

The other question I should like to ask is: Considering the difficulty in estimating intensity of reaction, how important do you consider that variation?

DR. BÉLA SCHICK, New York: Did you get any entirely negative reactions?

DR. A. C. MCGUINNESS, Philadelphia: We have not used the heat-labile and heat-stabile fractions.

In regard to retesting over the same areas, that is one of the explanations we have offered for the variation. We were performing about 500 tests with Dick toxin every three or four days on these persons, and it is very likely that in a number of cases the tests were superimposed.

In regard to the importance of the intensity of the reaction, I feel that it is a very important factor. We have had many experiences to indicate that different reactions may have similar dimensions but exhibit wide variation in intensity. What is needed is a color standard to assist in interpreting the intensity of the reaction.

Dr. Schick asks whether or not we get complete reversal of the reactions. In younger children, say children up to 10 or 15 years of age, employing 30 cc. of pooled adult serum, we will get on the average a depression of sensitivity below the 20 lines, which lasts for about a week to ten days, and then the reaction comes up into the positive range again. This group was an older group, and I believe that one would have to employ a good deal more serum to get the same results. McKhann in his work on the oral administration as well as the intramuscular administration of placental extract found that he could not get nearly such consistent results in the older adult group as he could in children. We felt that this group was satisfactory because, even though we did not get a depression into the completely negative range, there was a definite effect following administration of the serum.

USE OF A GLOBULIN EXTRACT OF IMMUNE ADULT BLOOD IN PROPHYLAXIS AGAINST MEASLES. DR. S. KARELITZ, New York.

This article will be published in full, with discussion, in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

EFFECT OF DIET ON RESISTANCE TO INFECTION: I. MATERNAL DIET. DR. C. F. CHURCH and MISS CLAIRE FOSTER, Philadelphia.

The host resistance of a total of 1,842 mice of three inbred lines has been tested by Webster's technic, using Salmonella enteritidis as the test organism. The diets compared were a modified Steenbock diet (diet 200), the Sherman diet (diet 221) and a purified diet (diet 212) which was modified by adding or subtracting individual food elements. Survival on the "adequate" purified diet was similar to that on the natural foods, but reducing the mineral content to one fourth diminished resistance to a significant degree.

The diet of the mother during pregnancy and lactation was found to have an important influence on the survival of her progeny following their inoculation at 8 weeks of age. Progenies of mothers fed diet 200 were compared with those from mothers fed diet 221, all these animals being changed to the purified diet two weeks before inoculation. In one such comparison, 55 animals born of mothers on diet 200 showed 34.6 per cent survival four weeks after inoculation, while 44 animals born of mothers on diet 221 showed 9 per cent survival. The odds against this difference being a chance result are 370:1.

The descendants of a single litter have been followed through three generations on diet 200 as compared with three generations on diet 221. The first generation of offspring on diet 200 gave 24 per cent survival as compared with 13 per cent on diet 221; the second generation, 37 as compared with 14 per cent; the third generation, 46 as compared with 6 per cent. This increasing resistance with successive generations on diet 200 suggests that maternal diet may play an important rôle in the development of resistant and susceptible stocks.

DISCUSSION

Dr. G. M. Guest, Cincinnati: In a study such as this, in which an examination is made of various dietary factors entering into susceptibility to infection, the possible rôle of anemia should at least be considered. In two important studies, one by McKay in London and one by investigators in this country, a close correlation was found between morbidity and hypoferric anemia. The possibility of iron deficiency in the litters of young animals should therefore be given consideration in these experiments.

Dr. H. L. Hodes, New York: Were the spleens of the animals which survived tested for the presence of organisms? Were specific antibodies demonstrated in their serums?

Dr. C. F. Church, Philadelphia: The possibility of the diet of whole wheat flour and whole milk powder producing anemia has been considered. Growth and reproduction on this diet are essentially the same as on diet 200, as has been shown by the studies made in our laboratory by Miss Claire Foster. The survivors in each case have been examined after death. The spleen was cultured, and positive cultures were tested for agglutination with the immune serum.

Opsonocytophagic Test in Cases of Pertussis and in Cases of Children Vaccinated with Antigens of Haemophilus Pertussis. Dr. Charlotte Singer-Brooks and Dr. J. J. Miller Jr., San Francisco.

The recent adaptation of the opsonocytophagic test to the study of pertussis is scrutinized and the recent findings of Kendrick, Gibbs and Sprink are in general confirmed. These are: In infants and children after injection of a vaccine of Haemophilus pertussis in phase I there is a definite increase in phagocytosis of the organisms in vitro. The high opsonocytophagic titer is maintained for at least from six to nine months. During and after an attack of pertussis there is a similar rise in the phagocytic activity of the blood. A low degree of phagocytosis of these organisms is found in the blood of infants under 18 months of age when they have had neither the vaccine nor the disease. In children over 18 months of age more phagocytosis may be occasionally observed even though the history indicates that they have not had whooping cough. It is, however, rarely as marked as after vaccination or disease.

In addition the following was noted. After injection of H. pertussis undenatured bacterial antigen, no increase in the phagocytosis of the organisms occurred. Titers similar to those in the nontreated controls of the same age range were obtained. After injection of a vaccine made from mixed cultures of bacteria from the respiratory tract an increase in the phagocytosis of pertussis organisms occurred. This stimulation of nonspecific opsonins indicates that the test is not specific for opsonins of H. pertussis. This finding, however, does not necessarily invalidate the test, since an increase of nonspecific opsonin may be commonly associated with an increase in resistance. Variability in the ease of sensitization and phagocytosis by the same blood was noted with different phase I strains and with the same suspension of one strain as it aged. This together with other technical variables constitutes a drawback to the opsonocytophagic test in its present form.

DISCUSSION

Dr. W. L. Bradford, Rochester, N.Y.: My colleagues and I have been interested in the opsonocytophagic reaction of the blood in pertussis for some time. Our method and some of our results have been very similar to those described by Dr. Brooks.

I think it is a reaction that is valuable for the study of a trend rather than for any individual test. Study by this method is as dependable as the study of any other humoral antibody in pertussis. It may have certain advantages.

There are several weak points about the reaction. In our work, the presence of so-called normal opsonins has interfered somewhat. By diluting the serum and by using the leukocytes of a newly born infant, this particular objection may, we believe, be ultimately corrected.

Our interest has been confined chiefly to the effect of adult immune or of convalescent serum on the reaction. We have found that both definitely increase the phagocytosing power of the blood against the antigens of H. pertussis. Another interesting aspect of the problem which lends itself to study by this method is the matter of placental transfer of the antibody.

SELF SELECTION OF DIETS BY RATS. DR. C. P. RICHTER, DR. L. E. HOLT JR. and MR. B. BARELARE, Baltimore.

The purpose of these experiments was twofold: to throw light on optimum diets and to study appetite as a physiologic mechanism. There are numerous observations on record that animals suffering from dietary deficiency will make a correct choice of foods when the opportunity is offered. L. J. Harris, who made extensive studies of diets chosen by B deficient rats reached the conclusion that the correct choice depended on the experience of the animal rather than on instinctive craving, and that, furthermore, the rat seemed able to choose correctly only natural foods; the B deficient animal failed to select a diet containing this vitamin when it was added in the form of a highly purified concentrate. The observations which we have made do not support Harris' conclusions.

We have offered rats a choice of from 8 to 10 different foods, using almost exclusively pure substances rather than mixed diets. The rats were able to select proper amounts of protein, carbohydrates, fat, minerals and vitamins for normal growth. Some of each material offered was taken, the chief variation in consumption being in the case of carbohydrate and fat. Here certain animals ("sugar burners") exhibited a marked predilection for carbohydrate whereas others ("oil burners") took little carbohydrate and consumed relatively large amounts of fat.

In animals with avitaminosis A it was found that when vitamin A was offered in the form of cod liver oil, the intake of this oil would after a few days rise far beyond the quantity consumed by normal animals, eventually returning to normal as the evidences of avitaminosis disappeared. This response could have been interpreted as the result of experience after trial of the new foodstuff.

Observations with animals deficient in $B_1$ yielded quite different results. When these animals were given access to yeast, the rise in yeast consumption was immediate, and when the vitamin was supplied in pure crystalline form the result was even more dramatic. An extraordinary craving for vitamin $B_1$ seems to exist in these animals, and as soon as a container with it is introduced the rats cannot restrain themselves. Such a craving can hardly be interpreted as the result of experience.

An interesting observation was made in regard to the fat and carbohydrate intake of these rats. It was found that during the stage of deficiency the appetite for carbohydrate and also for protein was greatly decreased, whereas the amount of fat consumed was considerably increased. The reverse change took place immediately after the introduction of the vitamin into the diet; there was a sharp fall in the consumption of fat and a rise in the intake of carbohydrate and protein. These results are in agreement with current views as to the rôle played by $B_1$ in the utilization of carbohydrate.

DISCUSSION

DR. L. E. FARR, New York: I should like to ask if there was any change in the activity or the clinical condition of the rats when they spontaneously changed from an oil-burning diet to a sugar-burning diet and vice versa.

DR. DOROTHY V. WHIPPLE, Philadelphia: My co-workers and I also have been working on the relation of vitamin $B_1$ to carbohydrate metabolism. We have

attacked the problem from an entirely different point of view. We have found that animals deprived of vitamin $B_1$ are apparently unable to use carbohydrate, and that when they are supplied with vitamin $B_1$ they are suddenly able to burn carbohydrate to a very remarkable degree. Dr. Holt's findings that animals deprived of vitamin $B_1$ do not voluntarily consume much carbohydrate is in harmony with our finding that they are unable to use it.

DR. A. H. WASHBURN, Denver: In corroboration of Dr. Holt's point about the rats being able to choose what was lacking in their diet, my associates and I two or three years ago in Denver had a group of rats that were on a diet producing anemia. They were in glass cages, cages made with wood and glass rods, because it was noted that when they became anemic, if there were any nails or iron in the cage, they would gnaw these. That has been observed elsewhere, but we were particularly interested in two or three rats which succeeded in breaking through their cages when they became quite anemic, and we found that both copper and iron apparatus around the laboratory were chewed during the night quite extensively, enough to produce a very significant increase in the hemoglobin.

DR. C. F. CHURCH, Philadelphia: It appears that the voluntary selection of fat by these animals deprived of vitamin $B_1$ with the carbohydrate in the diet low is in direct confirmation of the sparing action of fat on vitamin $B_1$. I should like to ask if there was any indication of a change in the storage of fat after the addition of yeast to the diet.

DR. L. E. HOLT JR., Baltimore: The difference in behavior of rats eating predominantly one or another foodstuff is best illustrated by some curves which I shall show of animals which had access to only a single type of foodstuff and activity of which was recorded on a treadmill. On sugar alone the rats exercised to practically a normal extent; their activity was far less on a diet of pure olive oil and still lower on a diet of pure casein.

Dr. Whipple's observations on the respiratory quotient are quite in accord with ours as to the intimate relation between vitamin $B_1$ and the combustion of carbohydrate.

In my opinion there is no conflict between the view that vitamin $B_1$ is essential for the utilization of carbohydrate and the observations of Evans and Lepkovsky indicating that fats spare $B_1$. The explanation of the $B_1$-sparing effect of fats seems to be that on a high fat diet less carbohydrate is consumed and on that account less $B_1$ is required.

THE PASSIVE TRANSFER ANTIBODY: FLUCTUATIONS OF TITER IN TREATED AND UNTREATED HAY FEVER. DR. W. M. SCHMIDT and DR. V. W. LIPPARD, New York.

The purpose of these studies was to titrate the passive transfer antibody of patients with pollen sensitivity at certain periods with relation to the season of pollination in order to determine: (1) changes of titer in the absence of contact with the specific antigen, (2) the effect of treatment on titer and (3) the relation of titer to clinical result.

The method of titration was that of neutralization, previously reported before this society. The patients studied consisted of 18 treated ones and 10 controls. Twenty-six of the 28 patients were previously untreated. Titrations were performed before treatment, at the beginning of the season of pollination and at the end of the season of pollination.

The titrations define the range of titer in previously untreated patients and indicate that in the absence of contact with the specific antigen the titer remains relatively constant over a period of several months.

Treatment with the specific pollen produced a rise in titer in 16 of 18 patients.

There was no evidence of a correlation between the amount of treatment and the clinical symptoms, or the degree of rise of titer.

There did appear to be a correlation between the preseasonal level of titer and the severity of clinical symptoms, so that the patients with higher titers evidenced a greater degree of protection against symptoms of hay fever.

DISCUSSION

DR. J. D. TRASK, New Haven, Conn.: Do the results have any relation to the age of the patient?

DR. W. M. SCHMIDT, New York: No correlation could be found between the age of the patient and the titer reached, although the total group was so small that when it was broken up into age groups, only a few were in each group.

DIAGNOSIS OF CONGENITAL SYPHILIS IN THE NEW-BORN INFANT: THE QUANTITATIVE WASSERMANN TESTS AS A METHOD OF STUDY. DR. A. U. CHRISTIE, Baltimore.

This article will appear in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

ALTERED LIPID METABOLISM IN INFECTIONS OF CHILDREN. DR. A. V. STOESSER, Minneapolis.

In previous communications I have reported the influence of acute infection on the plasma lipids of children ranging in age from infancy to 14 years. There was a definite lowering of the values for the plasma lipids at the height of the disease as compared with the levels during convalescence. Diet had no demonstrable influence. The drop in the total fatty acids of the plasma was accompanied by a decrease in the iodine absorption values. This altered condition yielded an average iodine number of the serum fatty acids significantly lower during the febrile period of the illness, indicating that as an infection progresses the shift is from unsaturated to saturated serum fatty acids. This change also occurred in infants and children with such conditions as eczema in spite of the fact that the iodine number was already lowered in many of the cases. The fall in plasma phospholipids was associated with an initial rise in the iodine number of the phospholipid fatty acids and then a rapid decline to subnormal values. The reduction in the total plasma cholesterol was found to be due to a marked fall in the ester cholesterol, the free cholesterol content of the blood serum undergoing little change.

There was a tendency for the lipid content of the blood plasma to rise very slowly and to remain below the normal range during the period of recovery as long as any infection was present. This state of the plasma lipids during an illness in the child has been found to be quite similar to the changes which have been observed by Chaikoff and Kaplan in the blood lipids of depancreatized dogs maintained with insulin. The depancreatized dogs showed a moderate decrease in blood fat, a small drop in the plasma phospholipid values and a marked fall in the total cholesterol due almost entirely to a reduction in ester cholesterol to the point of disappearance from the blood in some of the animals. The free cholesterol content of the blood serum changed little. When raw pancreas was included in all diets fed after pancreatectomy, a rise instead of a fall in the blood lipids occurred. In view of this observation, it was thought to be worth while to feed fresh raw pancreas to children harboring an infection and demonstrating subnormal lipid values in order to determine whether the glandular tissue was capable of favorably influencing the disturbed lipid metabolism so that a return to normal would occur more rapidly. Up to the present time 6 children have received the fresh raw pancreas over periods of from six to eight weeks and the results are encouraging enough to warrant further studies. Fortunately, desiccated whole beef pancreas which has been dried at about body temperature and which has had the fat removed by extraction with gasoline is now available. This preparation can be offered to the child in fairly large amounts before any objection to it occurs.

DISCUSSION

DR. L. E. HOLT JR., Baltimore: I should like to ask Dr. Stoesser to what extent he believes that the low fatty acid content of the serum and the low iodine value of the serum at the height of acute infection are due to the increased utilization of unsaturated fatty acids that accompanies the increase in metabolic rate.

DR. A. V. STOESSER, Minneapolis: I believe Dr. Holt is correct in stating that the utilization of the unsaturated fatty acids is greater during the acute stage of an infection when a high fever is present, but this does not explain why some of the patients have very high iodine numbers during the first few days of the infection.

## Afternoon Session

ORIGIN OF VITAMIN D AND ITS RELATION TO SOLAR RADIATION. DR. H. H. DARBY and DR. H. T. CLARKE, New York.

After the discovery of the rôle played by ultraviolet rays in the activation of ergosterol to form a crystalline preparation of vitamin D (calciferol), there have been a number of attempts to trace the origin of vitamin D in fish livers. To this end several investigators have examined marine plankton for antirachitic activity, with uniformly negative results. All the studies reported so far, however, have been carried out in temperate waters and usually in the winter months. It seemed to us that the irradiation in these regions at such times would be of extremely low intensity in the shorter wavelengths. In view of the high intensity of ultraviolet rays in tropical sunlight, as previously determined, we examined the sargassum weed (Sargassum fluitans et natans), an abundant alga of tropical waters which floats at the surface of the sea and is thus exposed to maximum illumination. The oils obtained from this alga showed good antirachitic potency when tested on rats. This finding indicates the presence of a material resembling vitamin D in a form of plankton which is abundant and widely distributed. It also indicates that the ultraviolet rays in tropical sunlight are of sufficient intensity to activate suitable materials. This adequacy has also been shown by recent studies on the vitamin D content of fermented cacao bean shells after drying in tropical sunlight (Knapp and Coward: *Biochem. J.* **29**:2728, 1935). The abundance of the sargassum weed and its wide distribution furnish a reasonable explanation for the occurrence of vitamin D in any fish which depend, directly or indirectly, on tropical plankton for their food supply.

DISCUSSION

DR. A. A. WEECH, New York: I should like to ask Dr. Darby how much oil he can extract from 100 pounds [45 Kg.] of seaweed, wet weight. I should like to ask further whether irradiation by sunlight after the seaweed was removed from the water may not have contributed to the antirachitic potency of its oil.

DR. H. H. DARBY, New York: One hundred pounds of wet sargassum (96 per cent water) gave, roughly, 90 Gm. of oil, of which about one quarter was unsaponifiable. This, of course, was not all vitamin D, by any means. One fifth of it consisted of fucosterol, a sterol which has recently been isolated from the closely related alga Fucus.

The question that Dr. Weech has asked brings up a point which is of great interest to us because of our desire to fit together all the different phases of this work. Professor Clarke and his students have been studying the proteins of sargassum weed and have found them to contain almost all the amino-acids present in complete proteins. This would explain the adequacy of the weed for the support of the immense fauna that collects and lives on it as it is carried north by the Gulf Stream.

As regards irradiation, my preliminary experiments showed that if the weed is allowed to dry in the sun it loses all its potency. I tried to increase the potency by solar irradiation but succeeded only in destroying the vitamin. The material worked up was brought directly into the laboratory, where it received no further irradiation.

ESTIMATION OF VITAMIN D IN BLOOD SERUM: CLINICAL APPLICATIONS. DR. J. WARKANY, Cincinnati.

Now that vitamin D is being more widely used in the prophylaxis and treatment of rickets, it has become obvious that some of the conditions previously believed to be rickets do not respond to the specific treatment. These forms of rickets resistant to vitamin D therapy are probably not an entity, and their classification and pathogenesis are still obscure.

When patients with this type of rickets are given antirachitic treatment the question of their capacity to absorb or utilize the ingested vitamin D arises. In this situation estimation of the vitamin D content of the blood serum appears to be of some interest, because it indicates whether the viosterol administered has reached the blood stream or not.

The normal vitamin D content of the serum of children is about from 30 to 50 rat units per hundred cubic centimeters, since 3 or 2 cc. of serum is usually required to obtain 2 plus healing in a rachitic rat. Estimations of the vitamin D content of the blood serum were made for 4 children, all of whom had the following findings in common: (1) changes of the bones resembling rickets, (2) a normal renal function and (3) a low inorganic phosphorus content of the blood. It was shown that the vitamin D level was raised by the oral administration of preparations of viosterol or cod liver oil concentrates to values above the normal (from 100 to 833 rat units per hundred cubic centimeters) without raising of the inorganic phosphorus content of the blood serum and without healing of the rachitic process.

Therefore, it may be said that in certain cases of rachitic changes of the bones a low inorganic phosphorus content of the blood serum and a normal or increased vitamin D level may coexist for a long time. This should be borne in mind in the treatment of children with this condition in order to avoid possible damage. To know that there is no lack of vitamin D in the blood serum of these patients may also aid in the search for the cause of the hypophosphatemia in intractable rickets.

DISCUSSION

DR. B. KRAMER, Brooklyn: I wonder whether any of these patients came to autopsy and whether the diagnosis of rickets was confirmed morphologically.

DR. J. WARKANY, Cincinnati: So far as I know, these children are all alive. I do not know of any autopsy on any of them.

INFLUENCE OF EXPOSURE TO SUNLIGHT AND VITAMIN D ON LEAD POISONING IN RATS. DR. M. RAPOPORT and DR. M. I. RUBIN, Philadelphia.

A series of experiments was carried out in an attempt to explain the increased incidence of manifest clinical lead poisoning in children and infants during the summer months. Two possible mechanisms offered themselves in explanation of the sudden manifestation of the symptoms of lead poisoning coincidentally with the onset of summer.

First, it was possible that the increased quantities of porphyrin circulating in the body of the animal with plumbism could produce damage when photosensitized by solar radiation. Second, increased absorption of lead from the gastro-intestinal tract under the influence of the vitamin D activity of summer sunlight could occur.

In young rats receiving 1.5 per cent white lead in their diets, daily exposure to sunlight or the administration of cod liver oil produced intense lead poisoning.

as evidenced by failure to grow or by death. Control rats receiving a similar quantity of lead but kept in the dark were only moderately stunted in growth.

Young rats poisoned with lead until there was retardation of growth were not adversely affected by subsequent exposure to sunlight or the administration of cod liver oil after lead had been removed from their diets.

These experiments indicate that sunlight intensifies the poisoning in the animal ingesting lead by increasing the quantity of lead absorbed from the gastro-intestinal tract. Sensitization of porphyrins seems to play no part in the sudden manifestation of the symptoms of plumbism.

DISCUSSION

DR. H. JOSEPHS, Baltimore: Did you try the absorption of lead by any other route than the gastro-intestinal tract, for instance, the lungs? I wonder whether absorption by some other route would make any difference.

DR. M. RAPOPORT, Philadelphia: No, we did not.

DR. S. S. BERNSTEIN, Detroit: Was the calcium in the diet given to these rats in a minimal dose, I mean in just about sufficient quantity to cover the rats' requirements, or was the amount of calcium in the diet fairly high?

DR. M. RAPOPORT, Philadelphia: So far as I can make out, the diet was well balanced. It had an adequate amount of calcium for the rats' requirements.

DR. D. H. SHELLING, Brooklyn: I was rather puzzled when I first did experiments with lead on rats, about three or four years ago, to find that vitamin D, instead of benefiting the animals, did them harm. I had an idea that since calcium and lead behave alike in the body in some respects, when vitamin D was given the lead would be diverted from the blood into the bones. Actually, however, the animals did not do so well when fed vitamin D. After my paper was published I repeated the experiment and sent some blood to Dr. Blumberg for spectroscopic analysis for lead. The method, of course, is rough and is not very accurate, but on comparison of the two groups, the animals that had received no vitamin D and the animals that had received vitamin D, the latter were found to have more circulating lead in the blood than the former. I am not sure whether vitamin D produced increased absorption or increased retention, but, whichever was produced, the animals that had received vitamin D in addition to lead had more lead in their blood than the group that had received no vitamin D. Recently Dr. Sobel repeated the experiment, using a more sensitive method for the determination of lead in the blood, and found that the blood of animals that had received cod liver oil and viosterol contained many times more lead than did the blood of control animals that had not received vitamin D.

DR. H. H. DARBY, New York: May I ask at what age of the rats the solar irradiation was started?

DR. M. RAPOPORT, Philadelphia: The rats were fairly young, weighing from 60 to 100 Gm. We found that we had to use young rats to produce lead poisoning. If we started with rats that weighed much more than 120 Gm., they continued to grow well with from 1 to 1.5 per cent of lead in their diet.

DR. H. H. DARBY, New York: These data are significant. Recent work by Windaus and Bock (1937) has shown that in the skin of the very young animal the concentration of provitamin is higher than that in the skin of the older animal. A case in point is that of the calf, in which 0.68 per cent of the sterols of the skin consists of provitamin, while the skin of the cow has only a quarter of this amount, 0.18 per cent. These data would fit in with the hypothesis that in the older animal, regardless of the amount of irradiation, there is not enough provitamin to yield the vitamin and thus allow the reaction to take place which Drs. Rapoport and Rubin obtained with huge doses of cod liver oil or vitamin D.

AN UNFAMILIAR RACHITIC SYNDROME. DR. HARRIET G. GUILD, DR. J. A. PIERCE and DR. J. L. LILIENTHAL JR., Baltimore.

This report calls attention to a clinical syndrome which we have not encountered previously but which has been described in scattered reports of cases in the German literature (especially by Fanconi: *Jahrb. f. Kinderh.* **147**:299, 1936).

A girl aged 17 months had presented difficulties in feeding since the first few weeks of life. Although she had held up her head at 4 months, she had subsequently developed slowly, early showing signs of rickets, which had continued to increase in spite of adequate antirachitic therapy. Urinary frequency and constipation with a tendency to abdominal distention had always been present; when she was 6 months of age renal glycosuria was discovered. Thirst and polyuria later became prominent symptoms; vomiting was added to the difficulty in feeding, and there were frequent bouts of unexplained fever. The weight had been at a standstill for seven months, and tenderness on handling had been noted for two months, before admission.

Examination revealed: (1) poor nutrition and development (the weight was 16½ pounds [7.484 Gm.] and the length 31½ inches [80 cm.]); (2) signs of rickets (craniotabes, a rosary, thickened radial epiphyses, a kyphotic posture when sitting and inability to stand); (3) delayed dentition; (4) abdominal distention; (5) a large, hard liver with a "scalloped" edge; (6) a palpable spleen; (7) slight clubbing of the fingers and toes; (8) tenderness on handling; (9) albuminuria, with a few casts and cells in the urine, (10) marked glycosuria, with only an occasional trace of acetone in the urine, and (11) a prolonged clotting time (fourteen minutes).

Further investigation has yielded data of importance with regard to the following points:

1. *Glycosuria.*—This was definitely renal, with a "threshold" of less than 65 mg. per hundred cubic centimeters of blood and loss of from 20 to 30 Gm. of dextrose in the urine daily. Tests of the dextrose tolerance showed a marked rise, the dextrose level having increased from 60 mg. per hundred cubic centimeters (during fasting) to 180 mg. at the end of one hour, with a sharp fall (to 50 mg.) at the end of two hours.

2. *The Renal Function.*—The nonprotein nitrogen content of the blood was 30 mg. per hundred cubic centimeters; the excretion of phenolsulfonphthalein was 50 per cent in two hours; a test of the urine showed concentration to at least 1.015 (after correction for the sugar content).

3. *Rickets.*—Roentgenograms showed rickets, with fractures, and osteoporosis. The phosphorus content of the blood was 1.3 mg. per hundred cubic centimeters ±; the calcium content was 8 mg. ±, and there was a normal vitamin D content (determined by Dr. Warkany). The Hamilton test for parathyroid hormone was negative; the phosphatase level was 49.9 units per hour. A test of the metabolism showed a negative calcium-phosphorus balance.

4. *Acidosis.*—The carbon dioxide-combining power of the blood was 30 volumes per cent ±. No acetone bodies were present. Tests for other electrolytes of the blood showed only a slight increase in chlorides, *a suggestively significant increase in the total organic acid content* (a satisfactory determination has not yet been completed) and a content of total fixed base within the normal limits.

5. *Urinary Excretion.*—The volume of urine excreted was increased. The $p_H$ of the urine (averaging 6.5) was relatively high in relation to the degree of acidosis. Urinalysis showed large quantities of organic acid (twenty times the normal amount), a marked increase in the ammonia content and a relatively high phosphorus content. There were normal excretion of ether-soluble reducing substance and satisfactory conjugation of camphyl alcohol administered by mouth. The urobilin content was moderately increased.

*Comment.*—The rickets, which has increased under observation, is regarded as secondary to the chronic acidosis, which is probably dependent on a congenital

disturbance in metabolism, leading to an accumulation of organic acids. Most of the abnormal urinary findings represent efforts on the part of a congenitally disabled kidney to compensate for the acidosis. Although its function is fair, according to the usual tests, the kidney cannot secrete a sufficiently acid urine, and a defective tubular mechanism is evidenced by the renal glycosuria. The shape and consistency of the liver suggest that this organ is also playing a part in the general metabolic disturbance, but further studies now in progress will have to be completed before such conclusions can be drawn.

DISCUSSION

DR. J. B. PINCUS, Brooklyn: The case that Dr. Guild has just presented resembles a case which my associates and I have been observing for the last fifteen months. Our patient is an older child. Almost all the cases of this disorder have occurred in girls, except 1, that of a brother of the patient, who was not examined and who died at the age of about 4 months of apparently the same condition. Otherwise, all the cases of this condition so far reported have occurred in very young girls. Our patient had no rickets or evidence of rickets during the first year of life. She was under the care of competent physicians and until the age of 2 years was considered perfectly well. After her second year she began to show disinclination to walk and gradual bowing of the extremities. Roentgen examination of the long bones showed rickets. She had, and still has, in common with the other patients with a similar condition, hypophosphatemia, glycosuria, albuminuria and casts in the urine. The renal function is perfectly normal. The blood pressure is normal, and there is no increase of the nonprotein nitrogen content of the blood. One interesting feature, which was not observed in the patient reported on by Dr. Guild, is that her respiratory quotient is that of a true diabetic patient. It falls between 0.71 and 0.75, and her curve for sugar tolerance is also more like that of a diabetic patient.

Our metabolic observations differ from those of Dr. Guild and her collaborators. Some response to very large amounts of vitamin D was obtained in that a previously negative balance of lime salts became positive. Even so, the retention was not so great as one observes in a child with active rickets. All attempts to cure the rickets in this patient have failed so far. However, her general health is good, and she is apparently growing in height and gaining in weight. These features are in marked contrast to the case just reported and to those described by other observers.

What the nature of this disturbance is I am at a loss to say. The patient does not have acidosis. The disease is certainly not renal rickets. Our patient is not dwarfed, and in this respect again she is different from the patient described by Fanconi. Apparently we are dealing with some peculiar disease which has just recently been called to the attention of the medical profession. This is a form of rickets which is associated with a disturbance of the carbohydrate metabolism; it may be severe, as in the cases reported by Drs. Guild and Fanconi, or mild, as in our case.

DR. G. M. GUEST, Cincinnati: There are two features in this case which I should like to discuss briefly. I have not had occasion to observe a patient with this condition, but I have been anxious to see measurements of the ester phosphorus content of the blood cells made on one of them. With any fixed acidosis there should be a great decrease in the ester phosphorus content of the blood cells. This finding may be of more than academic interest, as all the members are familiar with Robison's argument that calcification of bone takes place through intermediate metabolism of the ester phosphorus rather than through metabolism of the inorganic phosphorus of the blood serum alone. It would be interesting to know whether in the presence of this acidosis the ester phosphorus content of the blood cells is significantly lowered.

Again, if I understood one of the charts correctly, although the urinary function was reported to be not markedly diminished, I believe 50 per cent of the

phosphorus content of the stool is still in excess of the urinary phosphorus content. In a normal child with good urinary function, if phosphorus is being absorbed from the intestinal tract the urinary phosphorus content should be in excess of the phosphorus content of the stool, and even though the renal function appears to be normal there may still be relative inability to excrete phosphorus in the urine.

Dr. S. Farber, Boston: I should like to ask Dr. Guild if a primary tumor of the liver has been excluded. I mention that because my associates and I observed a case a few years ago in which severe rickets of this type was observed and in which at operation and autopsy a large hepatoma was observed, occupying about four fifths of the liver.

Dr. E. A. Park, Baltimore: Cases of rickets such as those just described, in which the condition depends on some factor other than vitamin D deficiency are very interesting. It is apparent that the condition exists and it is coming to light in more and more definite form.

The whole subject is baffling. Dr. Shelling in his studies of the effects of viosterol in the cure of rickets has found several older children with rickets whose condition yielded when vitamin D was given, but only when very large doses were employed.

Dr. Butler and Dr. Albright have had a patient in Boston, 15 years old, who appeared to be refractory to vitamin D therapy. It was impossible to distinguish the condition from ordinary rickets due to vitamin D deficiency except in the refractoriness to treatment. One hundred and fifty thousand U. S. P. units of vitmin D daily was without effect. Dr. Albright obtained a toxic effect from vitamin D only when the dose was increased to 1,500,000 U. S. P. units daily. Then, I believe, the calcium content of the blood rose to a level above the normal. A healing process could be detected by the roentgen rays only when immense doses of vitamin D were given. The difficulty was not one of absorption, because when the vitamin was given parenterally it was not effective.

Dr. F. S. Smyth, San Francisco: I am sorry that I did not bring a slide showing the results of two years' observation of a 5 year old child with chronic rickets which suggest similarity with the condition reported by Dr. Guild. My recollection is that my associates and I found a bicarbonate content of the blood lower than the normal and slight albuminuria. I wonder if in Dr. Guild's case there was any indication of nephritic involvement with an excess loss of base by the urine.

Our patient responded when vitamin D was increased to a total of 50,000 U. S. P. units daily. The blood phosphorus rose from 1.5 to 5 mg. per hundred cubic centimeters during the period of observation of fourteen months.

Dr. B. Kramer, Brooklyn: I think that in cases of this type one should be careful about concluding that the patient is suffering from rickets solely because the roentgen picture closely resembles that of rickets. In the type of marble bones occurring in early infancy the roentgenographic picture has been diagnosed as showing rickets or, in the presence of a diffusely dense shaft, as indicating marble bones and rickets, but no evidence of rickets was seen on pathologic examination. This diagnosis seemed justified clinically by the additional finding of a normal or a slightly lowered calcium concentration of the blood, with a low inorganic phosphorus content yielding a low calcium-phosphorus product. This patient was, however, resistant to antirachitic therapy. The disease known as renal dwarfism or renal rickets is now known, in at least some instances, to be due to a lesion which is not at all rachitic but more closely resembles osteitis fibrosa cystica and is associated with diffuse hyperplasia of the parathyroids.

Significance of the Respiratory Quotient During Fasting. Dr. E. M. Bridge, Baltimore.

It is well knowr from experiments on animals that a high respiratory quotient is induced by feeding foods rich in carbohydrate and that under such conditions the liver contains large amounts of glycogen; when the food contains little or no

carbohydrate, both the respiratory quotient and the glycogen content of the liver are low. That such associations are more than incidental is shown by studies on 120 normal rabbits in which a parabolic relationship was found to exist between the glycogen content of the liver and the respiratory quotient, provided the determinations were made under conditions of absorptive equilibrium.

In experiments on man in which diets were employed which gave varying levels of the respiratory quotient during fasting, it was found that the height of the curve for the capillary blood sugar content varied inversely with the respiratory quotient during fasting—a low respiratory quotient during fasting was associated with a large rise in the blood sugar content after the ingestion of dextrose, and vice versa. From this it is concluded that the respiratory quotient during fasting and the curve for the blood sugar content provide a means of determining approximately the glycogen reserve in man.

DISCUSSION

DR. A. A. WEECH, New York: There are two schools of thought concerning the physiologic disturbance which leads to diabetes mellitus. School A, as it may be called, the teaching of which is most generally accepted, assumes that lack of insulin leads to inability of muscles and other tissues to burn carbohydrate and that because there is no combusition of carbohydrate the respiratory quotient is low. On the other hand, school B does not suppose any interference with the combustion of carbohydrate as a cause of diabetes mellitus, but it does assume that transformation of fat into carbohydrate in the liver is pathologically abundant. Since the respiratory quotient is unity when carbohydrate is being burned and zero when fat is being converted, one can account for the low respiratory quotient in diabetes on the basis of a combination of these reactions.

The demonstration by Dr. Bridge of an important correlation between the respiratory quotient during fasting and the level of glycogen in the liver may be of help in deciding in which of the two schools of thought the truth lies. The demonstration suggests that the composition of the mixture which is to be metabolized is determined in the liver. If this is true, it is difficult to understand how muscles and tissues distant from the liver can decide of their own volition whether they prefer to burn sugar or fat. I wonder, then, if this work does not lend support to the teaching of school B, namely, that fat is first transformed into carbohydrate in the liver, that in the peripheral tissues the only material which serves as a source of energy is carbohydrate and that diabetes does not lead to impaired ability to burn sugar.

DR. D. C. DARROW, New Haven, Conn.: I wonder if Dr. Bridge has tried out these correlations on animals other than rabbits. It just occurred to me that because of the large stomach and intestines of the rabbit the findings for this animal may be somewhat peculiar.

DR. T. L. ALTHAUSEN, San Francisco: I have been interested for years in the glycogen content of the liver in various diseases, and all physicians have been handicapped by the absence of methods of determining the hepatic glycogen content in man. Many erroneous concepts are being repeated in edition after edition of textbooks. It is said, for instance, that the diseased liver is unable to store glycogen. I was able to persuade some of the surgeons with whom I am associated to excise pieces of liver during an operation when the condition of the patient was good, and we examined this material for glycogen. In this manner we were able to prove that the liver in hepatic disease is able to store glycogen. The low glycogen content of the liver in diseases of this organ appears to be in most cases a matter of deficiency of the total carbohydrate content of the body. If our patients were given an abundance of carbohydrate food or dextrose for several days before the operation we found as much as 10 per cent of glycogen in the liver. In comparable conditions without the previous treatment with dextrose the hepatic glycogen content amounted to less than 1 per cent.

I think this work of Dr. Bridge is very important, and I am eager to ask him whether he has tried his method in clinical conditions in which the hepatic glycogen content is known to be very low or unusually high, as in von Gierke's glycogen disease, in which the glycogen of the liver is supposed to be locked up and unavailable to the rest of the body.

Dr. J. W. Maroney, Detroit: Dr. Johnston and I did some studies somewhat along this line in which we obtained a respiratory quotient for a fasting subject and then gave an intravenous injection of dextrose and determined the respiratory quotient at hourly intervals after this. After the intravenous injection of dextrose we found a marked rise in the respiratory quotient and generally a corresponding increase in the percentage of carbohydrate burned. If, however, we took a starved subject (for instance, one child had hyperthyroidism, and another had an adhesion obstructing the ileum and had lost 40 pounds [18 Kg.]) the administration of dextrose was not followed by a rise in the respiratory quotient. Dann and Chambers (Dann, M., and Chambers, W. H.: Glycogenesis from Glucose Administered to the Fasting Dog, *J. Biol. Chem.* **95**:413, 1932) have shown that in fasting dogs dextrose that fails to be oxidized is accounted for as glycogen.

Dr. S. Z. Levine, New York: I think that the work has definitely shown a correlation between the state of the glycogen content of the liver and the respiratory quotient. Dr. Newburgh recently, without determining the glycogen content of the liver of the fully grown adult, made observations analogous to those of Dr. Johnston on children. They both found that apparently in the fasting state the human organism preferentially stores glycogen rather than burns ingested or intravenously administered dextrose. If a human subject has a low respiratory quotient during fasting, the quotient may not rise immediately after the ingestion or the intravenous administration of dextrose but may remain the same for from four to eight hours. The administered dextrose is apparently being stored in the liver, presumably as glycogen. Thereafter the respiratory quotient rises and follows the course that it normally would when the hepatic reservoirs are replete with glycogen. The relationship demonstrated by Dr. Bridge for animals therefore seems to hold for human beings, both children and adults. The question that some one raised about the use of other animals than rabbits is a good one, because of the facile and fluctuating carbohydrate metabolism in the latter animals, but the latter factor would probably not vitiate the reliability of the results in this instance.

Dr. E. M. Bridge, Baltimore: I think that Dr. Levine has already answered Dr. Darrow. I have not tried any other animals than rabbits, but, judging from the way in which the respiratory quotient of man during fasting is correlated with his preceding dietary state, it seems likely that a similar situation holds for other animals.

Dr. Althausen has asked about other diseases. I think I can say that in hyperthyroidism there is a tendency toward a low respiratory quotient during fasting under conditions in which the patient is losing weight and in which he cannot eat sufficient food to maintain his weight against an increased metabolism, and that as he improves after operation the respiratory quotient during fasting is higher and the curve for the blood sugar content lower.

I have studied only one patient with diabetes and have observed nothing unusual in that case. I have never had occasion to see a patient with glycogen disease. These findings add confusion to the classic ways of thinking with regard to the combustion of carbohydrate. The argument is a long one, and I should simply like to point out that the modern theories of the production of muscular energy, at least some of them, consider that muscular energy is derived not by oxidation but by splitting of creatine phosphate. This would correlate better with the present findings than other suppositions.

EFFECT OF THYROID ON THE NITROGEN BALANCE IN THE PERIOD OF GROWTH. DR. J. A. JOHNSTON and DR. J. W. MARONEY, Detroit.

Studies of the nitrogen balance were carried out in a cretin over a five month period during and following the omission of thyroid treatment, in 2 children with hyperthyroidism and in 2 children with normal basal metabolic rates, one an obese girl who was given large doses of thyroid and the other a child of normal weight who was given small doses of thyroid. In the cretin the administration of thyroid was accompanied by an increase in the nitrogen balance after an initial negative phase. In the child with severe hyperthyroidism positive balances were obtained with a high intake of thyroid, but more strongly positive balances were obtained after thyroidectomy. In mild hyperthyroidism higher nitrogen balances were obtained in subjects with higher metabolic rates than in those with lower metabolic rates. In a normal child an increase in the nitrogen balance was induced with an amount of thyroid small enough to produce only a slight increase in the metabolic rate. In the period of growth a positive effect on the storage of nitrogen is evident with the administration of thyroid in the normal child as well as in the child with hypothyroidism; whether this action is secondary to increased utilization of carbohydrate and fat or whether it involves a primary anabolic effect on nitrogen is not apparent.

DISCUSSION

DR. A. A. WEECH, New York: From the standpoint of the utilization of carbohydrate, protein and fat, is there a difference between the action of thyroid and the effect of dinitrophenol, which is also a metabolic stimulant?

DR. S. Z. LEVINE, New York: In one of the charts, I think the second, while the nitrogen balance is indicated as becoming positive and the metabolic rate as rising, the weight of the creatine is shown as decreasing, indicating paradoxically that the loss of weight might possibly have resulted from a loss of water or myxedematous tissue associated with storage of nitrogen.

DR. J. W. MARONEY, Detroit: After we discovered what had happened we were sorry that urinary outputs had not been measured and that studies of the water balance had not been made.

ERYTHROPHAGOCYTOSIS IN ANEMIA OF THE NEW-BORN: REPORT OF TWO CASES. DR. T. C. WYATT, DR. W. A. GROAT and MISS MARY B. COOPER, Syracuse, N. Y.

Three cases of severe anemia in new-born infants are described. In two of the infants definite phagocytosis of erythrocytes in the circulating blood was found. In the third infant, who was seen earlier after birth than the other two, there was some evidence of such phagocytosis taking place.

The occurrence of erythrophagocytosis in infants is probably much more common than one would suppose from the descriptions of the only 4 cases of this condition which we have found in the literature.

Such phagocytic activity suggests a fundamental variation from the normal state on the part of either the erythrocytes or the phagocytes, possibly related to development. Its occurrence may offer some evidence as to the mechanism underlying rapidly developing anemia of the new-born, with or without jaundice. The phagocytosis itself does not seem important in the production of such severe anemia as was present in these cases.

In one infant who was examined at autopsy (the other 2 recovered) there was no evidence of erythrophagocytosis in the tissues. The spleen, however, showed considerable pigmentation, suggesting excessive hemolysis.

DISCUSSION

DR. C. H. SMITH, New York: The supravital technic affords a direct approach to the examination of living blood cells as they appear in the peripheral blood. Over a period of many years in which this technic has been employed in a variety

of pathologic conditions in infants and children, I have observed erythrophagocytosis in specimens of blood but twice: in a case of myeloid leukemia and in one of severe anemia. The infrequency of this phenomenon as observed during this time, together with the relatively small number of recorded instances, leads one to suspect that the entrance of phagocytic cells containing erythrocytes into the peripheral circulation is a rare occurrence.

It is important to recall that fragmentation and phagocytosis constitute the normal mechanisms by which destruction of red blood cells is effected. The former occurs within the circulating blood, and may be visualized in a drop of fresh blood, particularly when this process is exaggerated, as in instances of severe anemia. After the erythrocytes have been altered in this manner, they are disposed of by phagocytosis within the reticulo-endothelial system, ordinarily during passage through the spleen. In one of the cases presented by Dr. Wyatt, however, in which autopsy material was available, the most prominent areas of erythrophagocytosis appeared within the mesenteric nodes.

From what has been stated, it is improbable that erythrocytes are ingested in the blood stream. If such ingestion did occur in the cases reported, the degree would still be insufficient to account for the anemia. It is more likely that the erythrophagocytosis observed in these cases represents the accidental spilling over into the circulation of phagocytes containing red cells from tissues where this method of destruction of blood was in active progress. It is conceivable, however, that the erythrophagocytosis in these and in previously reported cases of anemia of the new-born indicates that erythrocytes are removed from the circulation to an abnormal extent by phagocytic cells within the reticulo-endothelial system, which contributes to lowered values for erythrocytes.

Dr. A. H. Washburn, Denver: I have seen phagocytosis of red cells by large mononuclear cells in a number of cases of various conditions, including several cases of leukemia and 2 cases of Hodgkin's disease, but what seems to me of somewhat greater interest is that I have twice seen it in apparently healthy new-born babies, babies whom I have had the opportunity of following for six or eight months subsequently. They had no anemia, had normal findings for the blood and were healthy in every way.

I wonder perhaps if the explanation is not that phagocytosis of red cells may go on under varying conditions, but that it is only when abnormal white cells are spilling into the circulation, which certainly takes place in the early neonatal period and in various diseases, that one finds phagocytosed red cells appearing in the circulation.

Lipid Partition of Erythrocyte Stroma. Dr. S. S. Bernstein, Miss Betty N. Erickson and Mr. H. H. Williams, Detroit.

Stroma was prepared by hemolyzing washed erythrocytes in 20 volumes of distilled water and buffering the mixture to a $p_H$ of 5.5 with a citric acid-sodium citrate buffer. The stroma was thrown into a Sharples centrifuge having 35,000 revolutions per minute and washed from three to six times in a buffer solution (of $p_H$ 5.5). It was then dried in a vacuum oven at 30 C. Samples of stroma were prepared from the erythrocytes of the cow, sheep, horse, chicken and turkey and of man.

The contamination of these preparations by hemoglobin was calculated from their content of organic iron, which varied from 2.4 per cent in the sheep to 17.74 per cent in man.

The protein present was calculated from the nitrogen content as determined by the micro-Kjeldahl method of Van Slyke. Protein other than hemoglobin makes up from 52 to 68 per cent of the mammalian stroma and 87 per cent of the avian stroma.

The values for the lipids were determined by the methods of Kirk, Page and Van Slyke. The lipids make up most of the remainder of the stroma. Practically all the lipid was found to be in the form of phospholipid and cholesterol. The

total lipid content of the stroma showed considerable variation, ranging in mammals from 25.6 per cent for the cow to 11.2 per cent for man. The lipid content of the avian stroma averaged only 2 per cent, but this might be expected, since the avian stroma is made up largely of nuclei of cells.

Within the individual species the values for lipid showed a remarkable consistency, varying in three different beef preparations only from 25.4 to 25.9 per cent and in three human preparations from 10.4 to 12 per cent. The values for the total lipid content of the intact cells showed no correlation with the values for the total lipid content of the stroma, being higher in the human erythrocyte, which has a stroma of lower lipid content, than in the red cell of the cow, with its high lipid content. The percentage distribution of the various lipid components in the stromata were similar to the distribution in the intact cells.

The phospholipid fraction was studied by determining the carbon-phosphorus ratios on the isolated phospholipids. These values, except in the avian stroma, fall within the limits of the theoretical values of lecithin, cephalin and sphingomyelin. After saponification the carbon-phosphorus ratios for the fatty acids were determined and compared with the theoretical values. These indicated that the phospholipids of the stroma of the cow and of that of the sheep are largely of the lecithin-cephalin type, while those of the human stroma are sphingomyelin.

DISCUSSION

DR. W. W. SPERRY, New York: I noticed that in the analyses of both the stroma and the erythrocytes Dr. Bernstein and his collaborators obtained values for cholesterol esters ranging from zero up to, roughly, about 25 per cent of the total cholesterol content, if I remember their figures correctly. It has never been adequately settled whether there is any cholesterol ester in red cells. Brun, in a recent publication from Dam's laboratory in Copenhagen, reported values which were constant from person to person and showed pretty definitely, I felt, that no cholesterol ester whatever is present in red cells. My associates and I made a few analyses some time ago, which also indicated the same thing. I am wondering whether the values for cholesterol ester obtained by Dr. Bernstein and his collaborators may represent experimental error or whether there really was cholesterol ester in either the stroma or the erythrocytes.

DR. M. J. E. SENN, New York: Having had some experience with this method of determining the value for plasma lipids, I think it is interesting to note the constancy of the values that Dr. Bernstein and his collaborators found for the stroma lipids. First, there is the difficulty, as was pointed out, in the washing of the cells. One would expect the amount of hemoglobin remaining and the amount of lipid lost to be variable. Were determinations of the lipid content made on the washings?

Second, the difficulties with the methods of the analysis of lipid used (especially the method for determining the value for cholesterol) are so numerous that greater variability in the figures of each series would be expected.

I am sorry that Dr. Van Slyke left the meeting without discussing these difficulties with his method.

DR. S. S. BERNSTEIN, Detroit: In regard to the question about the cholesterol esters, the only preparations in which we obtained high values for cholesterol esters were the avian cells, and we feel that we found such a small amount of lipid in those samples that these values could well be due to an error. The values for cholesterol esters of the other preparations are within the limits of experimental error, being only 1 or 2 per cent.

Of course, every one knows the difficulty that we have had so far with the method for determining the value for cholesterol. We have used a slight modification of Van Slyke's method of precipitation with digitonin, which has so far yielded rather constant results.

EXPERIMENTAL PULMONARY EDEMA. DR. S. FARBER, Boston.

In a recent communication we concluded from experiments on rabbits and guinea-pigs that the severe pulmonary edema which occurs shortly after bilateral cervical vagotomy is dependent on disturbance of the vasomotor control of the pulmonary vessels. Other factors also initiated by bilateral vagotomy are not essential to the production of this type of pulmonary edema. Attention was called to the occurrence of a similar type of pulmonary edema in man, found most often in association with certain diseases of the central nervous system. It was concluded that disturbance of the vasomotor control of the pulmonary vessels, caused by disease of either central or peripheral nerves, may be responsible for serious alterations in the dynamics of the pulmonary circulation and in the integrity of the pulmonary vessels. Such alterations lead to pulmonary edema. To connote the pathogenesis the term neuropathic pulmonary edema is employed.

Evidence pointing to a marked increase in the permeability of the pulmonary capillaries as a consequence of bilateral cervical vagotomy has been obtained by several methods. Trypan blue injected into the veins of the ear of rabbits at the height of the experimentally produced edema passes rapidly into the air spaces and upper respiratory tract and colors the frothy edema fluid a blue visible to the naked eye. In agreement with the findings of Kraus, it was noted that severe pulmonary edema is produced and death occurs in the recently vagotomized rabbit within a few minutes after the rapid intravenous injection of physiologic solution of sodium chloride in amounts which have no effect on the lungs of a rabbit with intact vagus nerves. In these experiments it is probable that several factors, which are being analyzed, are of importance in addition to the primary disturbance of the vasomotor control of the pulmonary vessels occasioned by bilateral vagotomy.

The serum protein level was usually appreciably reduced. The reduction was gradual and paralleled the increase in severity of the pulmonary edema. A few determinations showed no differences in the values for serum protein in samples taken from the pulmonary veins and samples taken from the superior vena cava at the height of the edema. The edema fluid had a protein value lower than, but approaching, that of the blood serum. Observations made with Drs. John Gibson and T. H. Ingalls demonstrated that during the development of neuropathic pulmonary edema in rabbits, the plasma volume, the total blood volume, the red cell volume and the hematocrit reading become considerably reduced. The lowered values for the blood plasma and for the total volume of blood may be correlated with the loss of fluid from the blood stream into the lungs. The inconstant reduction in the red cell volume (hemoconcentration occurs more frequently) is explained by hemorrhage into and from the lungs, which occurs in some experiments as a complication of the severe edema and congestion.

DISCUSSION

DR. G. M. GUEST, Cincinnati: I should like to ask whether you can by these observations relate the syndrome of acute tracheal bronchial edema to a nervous disorder.

DR. S. Z. LEVINE, New York: I should like to ask whether an attempt was made to determine the protein content of the edema fluid.

DR. A. A. WEECH, New York: I should like to ask whether any observations on the intrapleural pressure were made.

DR. S. FARBER, Boston: Answering Dr. Guest's question, we have in several cases gathered evidence histologically and grossly of definite damage to the medulla and to the nuclei of the vagus nerves in instances of severe pulmonary edema of the type he has mentioned. The level of the protein in the edema fluid was less than that of the protein in the blood; it was found to be about 4 Gm. per hundred cubic centimeters in several observations, as compared with from 5.5 to 6.5 Gm. in the blood serum.

We have not yet measured the intrapleural pressure, Dr. Weech. These experiments are being continued.

LIPOID CELL PNEUMONIA; A NEW METHOD OF IDENTIFYING THE OIL IN THE LUNG.
DR. I. J. WOLMAN and DR. H. STEVENS, Philadelphia.

In reviewing autopsy material at the Children's Hospital of Philadelphia, our attention was directed to a number of lungs with lipoid pneumonia. The characteristic macroscopic appearance was that of yellow or grayish yellow pulmonary deposits in a variety of sizes and shapes. Microscopically the alveoli were seen to be filled with fat-containing mononuclear cells and free globules of oil. The distribution of the lesions indicated the exogenous origin of the lipoid. The posterior dependent parts, especially the perihilar regions, were involved. The right lung was more involved than the left in every case. The nodules and solid lobules of lipoid pneumonia were confluent, grouped or widely separated. In anesthetized animals similar pulmonary deposits have been produced by the instillation of various oils into the nostrils.

Our series includes 30 patients with lipoid pneumonia, in 25 of whom the disease was fatal; 23 were studied at autopsy. No case was included in which the accompanying presence of amorphous coagulum suggested recent aspiration of vomited milk. The majority of the patients were infants. In two thirds of these associated debilitating disease or constitutional deficiency was present. The majority of the infants had been given cod liver oil; only 3 had received nose drops of liquid petrolatum for any length of time; these 3 had also received cod liver oil by mouth. The clinical data were, as a rule, not adequate to furnish the desired information regarding the source of the aspirated oil.

It occurred to us that analysis by the ultraviolet method of fluorescence could be applied to the postmortem material. This method is based on the property of certain substances to convert ultraviolet rays into visible rays of characteristic color. Cod liver oil has a yellow fluorescent color; pharmaceutic mineral oil is either colorless or pale gray.

Studies were made in a dark room with a standard classroom carbon arc microprojector enclosed in a simple black metal shield. Carbons of the Everready C and K types were installed, and the glass lenses were removed. The visible rays were removed by the introduction of a "heat resisting red purple ultra" Corning glass filter. To determine whether the oils would retain their fluorescent qualities after introduction into the lung, we produced experimental lipoid pneumonia in a large number of rabbits and rats by instilling cod liver oil and mineral oil intranasally. The animals were killed after varying periods ranging up to four months. In every instance a clear color effect was elicited. The patches of pneumonia due to cod liver oil glowed with a clear yellow fluorescence, whereas the deposits of mineral oil were pale gray-white or gray.

In 14 of the patients the consolidated areas of the lung had yellow tints varying from ivory to orange brown. In 7 cases the consolidation was gray or gray-white. In two sets of lungs certain patches were yellow, while others were gray-white. Some of the difficulty in the human material may be attributed to the long interval —up to five years in some cases—between the time of necropsy and examination with the ultraviolet method of fluorescence. Fixation in solution of formaldehyde also appeared to exert a deleterious chemical effect.

This abstract is intended to call attention to a new method of study which should be applied to fresh autopsy material. Conclusions regarding the etiology in our cases will not be attempted.

DISCUSSION

DR. S. FARBER, Boston: I think that it is important to continue to stress the danger of aspiration of oil into the lungs of children. In any autopsy service cases of such conditions are observed with regularity. I should welcome any method which would replace the methods that we used in determining the type of lipoid that one is dealing with.

DR. J. WARKANY, Cincinnati: I wonder if one could not devise a biologic test and examine the antirachitic value of the pulmonary tissue. If the pulmonary

tissue contains cod liver oil, it should heal rickets in rats when added to a rachitogenic diet.

DR. I. J. WOLMAN, Philadelphia: With a few exceptions, none of these children died of lipoid pneumonia per se. The pneumonia was noted more or less incidentally at necropsy.

GRANULOMATOUS ENCEPHALOMYELITIS DUE TO AN ENCEPHALITOZOON: A NEW PROTOZOAN DISEASE OF MAN. DR. A. WOLF and DR. D. COWEN, New York.

An infant born in New York of American parents and dying at 4 weeks of age had widely disseminated inflammatory lesions of the brain, spinal cord and retinas. These consisted of granulomas, massive areas of infiltration and necrosis, chiefly in the ventricular walls, and corresponding focal, meningeal inflammation. Similar lesions were present in the retina and choroid of each eye.

An organism approximately 1.5 by 3 microns in size, usually ovoid and having a polar mass of chromatin, was present in the lesions. It was most frequent where the process was most severe.

There is a striking resemblance between the granulomas in this case and those seen in epizootic encephalitis of rabbits and mice caused by Encephalitozoon cuniculi. The latter is considered to be a protozoan parasite probably of the order of microsporidia or haplosporidia. The organism in the present case closely resembles this parasite of rabbit encephalitis and must be a protozoan nearly related to it.

A condition reported by Magarinos-Torres from Brazil, also in an infant, in which similar organisms were present, appears to be the same disease. Jankû in Czechoslovakia reported retinitis in an infant similar to that in the present case, in which parasites also were present. It is of interest that Encephalitozoon encephalitis is common in rabbits in the area of New York and is endemic in many parts of Europe and America.

# News and Comment

## GENERAL

**Physicians Certified by American Board of Pediatrics.**—The following physicians have been certified by the American Board of Pediatrics since the last report:

Drs. Earl Hayes Baxter, Columbus, Ohio; Alfred DeBard Biggs, Chicago; Park Southworth Bradshaw, Ann Arbor, Mich.; Robert Peers Buckley, Duluth, Minn.; Edward J. Denenholz, Chicago; George Eisenberg, Chicago; Harry L. Faulkner, Chicago; Raymond F. Grissom, Oak Park, Ill.; Howard M. Jacobs, Chicago; Vernon E. Lennarson, Waukegan, Ill.; Benjamin Jacque Malnekoff, Milwaukee; Kenneth B. McDonough, Madison, Wis.; James Joseph O'Connor, East Chicago, Ill.; Mark F. Osterlin, Traverse City, Mich.; William Bernard Raycraft, Oak Park, Ill.; William Bryant Richards, St. Cloud, Minn.; Geneva Shong Rothemund, Springfield, Ohio.; Edwin Phillips Russell, Berwyn, Ill.; Josef Warkany, Cincinnati; Ernest Hamilton Watson, Detroit; David W. Whaley, Kitchener, Ontario, Canada.

These physicians were all examined. At this examination thirty-one men were examined; four failed, six were conditioned on one or more subjects and twenty-one passed.

## DEATHS

Prof. Johann von Bokay died on July 7, 1937, at the age of 79 years. He was known to a former generation as one of the outstanding pediatricians of his day. For many years he served as head of the pediatric department in the University of Budapest, Hungary, and he also served as an associate editor of the *Jahrbuch für Kinderheilkunde*. He was probably the best known of all Hungarian pediatricians. To one who visited his clinic he was most hospitable and kind, giving the impression of having unbounded energy and an active intellect.

## UNIVERSITY NEWS

Following a vote of the faculty of medicine of Bari, the ministry has chosen for the chair of clinical pediatrics of that university Prof. Bruno Trambusti, now at Parma.

# Book Reviews

**Handbook of Orthopedic Surgery.** By A. R. Shands Jr., in collaboration with R. B. Raney. Price, $5. Pp. 593, with 169 illustrations. St. Louis: C. V. Mosby Company, 1937.

This textbook is by far the most practical which has appeared for the teaching of orthopedic surgery to students and for the use of practitioners. Perhaps the most outstanding feature of the book, however, is the author's presentation of the fundamentals of diseases of the joints and their treatment. Twenty-four chapters have been written in accordance with the arrangement proposed by the committee of the American Orthopaedic Association for undergraduate teaching, and while this form is not perfect, it comes as near to a logical arrangement as is possible for this branch of surgery.

The subject-matter has been chosen to show the types of disorder with which the modern orthopedic surgeon is concerned and is not confined to the experiences of one physician. It is, instead, a composite of the accepted teachings on this subject by contemporary specialists. Where controversial points arise the author displays a nicety of judgment between radical and traditionally conservative views in the specialty. This is obviously the result of impressions made on him during his own student career.

There are certain phases of etiology, pathology and treatment which vary with individual opinion; but in the main the contents of the book find general acceptance, and the points of difference are not of importance in teaching.

Included in this handbook are 169 illustrations, practically all of which are pen and ink drawings of original roentgenograms and specimens. Most of these excellent drawings have been carefully selected and for vivid expression are distinctly superior to the customary photograph or roentgenogram.

The chapters on tuberculosis, chronic arthritis and diseases of the lower part of the back are concise and well written. In the appendix there appears a fine bibliography arranged according to chapter.

The book has been completely stripped of long-winded description, and space is not consumed with discourse on the historical or developmental evolution of a particular affection, which would be of interest only to the more advanced student. This omission seems wise, especially when the available hours for teaching one branch of general surgery, important as it may be, are limited.

There is no other book which will give the student so much orthopedic surgery in such a concise and readable style.

**Recent Advances in Allergy (Asthma, Hay-Fever, Eczema, Migraine, etc.).** By George W. Bray, M.B., Ch.M., M.R.C.P., Physician in Charge of Children's Department, Prince of Wales Hospital; Assistant Physician, Princess Elizabeth of York Hospital for Children; Consulting Allergist, Children's Hospital, Hampstead; Clinical Assistant, Asthma Clinic, Guy's Hospital London. With foreword by Arthur F. Hurst, M.D., F.R.C.P., Senior Physician, Guy's Hospital; Chairman, Medical Advisory Committee, Asthma Research Council of Great Britain. Third edition. Price, $5. Pp. 517, with 107 illustrations. Philadelphia: P. Blakiston's Son & Co., 1937.

This is the third edition of "Recent Advances in Allergy" to appear within six years. Because of the confusion which still exists in the field of allergy, more investigative work is apparently being undertaken there than in any other field of medicine. Much of the confusion is probably due to the terminology used and its application to definite observations in laboratory and clinic. The author has attempted to clarify the situation in the opening chapter. The nature of hypersensitiveness and the differentiation between anaphylaxis and allergy are clearly and concisely brought out, illustrated with tabular statements. The book is divided into two general sections, the first dealing with allergy in general, and including

discussions of the various factors which are either primary or secondary in the precipitation of allergic manifestations, and the second, with the clinical aspects of the subject. The author has developed each of the clinical phases completely, particularly as to treatment. The sections on allergies to foods and cutaneous allergy are complete. The section on hay fever, although written primarily for physicians in England, is an excellent guide in the care of patients with hay fever, either in England or in the United States. The bibliography includes material published through the first half of 1936.

The book should be a valuable addition to the physician's library, both for general reading and for reference.

**The Avitaminoses.** By Walter H. Eddy, Ph.D., and Gilbert Dalldorf, M.D. Pp. 338, with 29 illustrations. Price, $4.50. Baltimore: Williams & Wilkins Company, 1937.

Dr. Eddy and Dr. Dalldorf have done an excellent piece of work in this presentation of present day knowledge of the vitamins. Each vitamin, except the little known ones in the vitamin B complex, is considered separately, and its chemistry, the clinical and the pathologic manifestations, both gross and microscopic, associated with its lack, the dosage and the methods of biologic assay are discussed.

The chapter on the relation of vitamins to infection is particularly sane, in view of the claims expressed in much of the literature. A summary of the point of view expressed is found in the following sentence: "We must search for vitamin defense mechanisms against infection in physiological effects on tissue cells whereby they are able to perform their normal activity, on their effect on the proper absorption and utilization of ingested foodstuffs and on their use to build certain neutralizing substances of a nature quite different from those listed in the bacteriologist's group of immunizing substances."

Another chapter suggests methods of further study of the relation of vitamins to the processes of disease. McCarrison, by copying deficient diets used by certain groups of persons, was able to produce the same morbid changes in animals as were common among the persons whose diets he copied. Rinehart found that a diet deficient in vitamin C, plus a streptococcic infection, produced in guinea-pigs lesions similar to those of rheumatic fever in man. The condition was not produced by the organisms alone.

The book may be highly recommended. It is well written; the type is good, and the illustrations are excellent.

**The Thyroid and Its Diseases.** By J. H. Means. Price, $10. Pp. 602, with 73 illustrations. Philadelphia: J. B. Lippincott Company, 1937.

This book is a definite addition to the literature on the thyroid gland. It is not simply a review of the literature, like so many books on the subject, but is a presentation of the personal experiences and ideas of the group of men working in the thyroid disease clinic of the Massachusetts General Hospital. Under the author's leadership, over a period of more than twenty years, this clinic has been one of the most productive in its field in the country. Not only has there been ample material for study, but the cases have been critically and experimentally studied.

The subject is presented chiefly in its practical and clinical aspects. The structure and the chemistry of the thyroid gland are discussed in relation to clinical conditions.

The author's theory of the action of iodine in hyperthyroidism is well presented. The subject of juvenile myxedema and cretinism is satisfactorily but rather briefly covered, as would be expected in a book of this sort. Iodine and endemic goiter are fully discussed.

The style is informal and clear and makes for easy reading. Illustrations are, in the main, sketches by the author. The bibliography placed at the end of each chapter is well selected, with no attempt at completeness.

This book can be recommended heartily as a sound, practical and interesting presentation of the subject.

**Care and Diet of Children.** By Harry S. Reynolds. Price, $2. Pp. 154. New York: Fortuny's, 1937.

This handbook for mothers uses the question and answer method. Its value to the mother may be judgd from the following illustration:

"264. What should be done when the baby has a cold in the head?

"At the onset give a cathartic: calomel (10 doses of one-tenth grain each at intervals of 10 minutes), castor oil or milk of magnesia. Give a hot bath, followed by a hot drink after 1 year (milk or lemonade), and put to bed, covering warmly with the object of promoting sweating. Vaseline or albolene (a few drops of the latter) may be put into the nostrils several times a day. The nose may be irrigated with a Seiler's tablet solution (one tablet to half a glassful warm water) morning and night, allowing repeated small quantities to run into each nostril, using a medicine-dropper and so tipping the head as to allow each instillation to run out before giving another. Keep the bowels open and keep the child at rest, preferably in fresh air, and avoid overfeeding. If he gets worse, having fever, or does not improve within a few days: Call a doctor."

**A Handbook on Diseases of Children, Including Dietetics, Welfare and the Common Fevers.** By Bruce Williamson. Second Edition. Price, $4. Pp. 329, with 62 illustrations. Baltimore: William Wood & Company, 1936.

This is a small textbook of pediatrics, and contains the usual material found in such a volume. All the necessary facts are given in a readable manner. It is well printed, and the illustrations are well chosen. To the reviewer's mind this is the best short treatise on pediatrics that has appeared to date. It should be invaluable to the student or practitioner who wishes his facts in compact form.

**Erbrechen im Kindesalter.** By Dr. Josef Siegl. Price, unbound, 4.80 marks. Pp. 90. Stuttgart: Ferdinand Enke, 1937.

The author discusses the various conditions in which vomiting is observed in the neonatal period, in infancy and in childhood. Acute and chronic forms of vomiting are considered separately, and both the common and the rare disorders are included. Emphasis is placed on differential diagnosis, but complete discussions of spastic pyloric stenosis, habitual vomiting in infancy, rumination and periodic vomiting are given. The material is well organized and is presented in an interesting manner.

**Bacteriology of Specific Communicable Diseases.** Issued by the Department of Public Health. Edited by M. S. Marshall. Pp. 141. San Francisco: J. W. Stacey, Inc., 1937.

This loose leaf pamphlet contains much useful information for one interested in the subject. It is practical and has much information to which one can easily refer.

The first part is taken up with the shipment of clinical specimens, with detailed information as to how this should be done. There follow a long chapter on the bacteriology of specific communicable diseases and one on the bacteria common to shellfish, to milk, to water and to sewage. There is a chapter on chemical procedures, and several appendixes on various subjects complete the pamphlet. The whole is carefully indexed.

**Elements of Orthopaedic Surgery.** By N. Ross Smith. Pp. 246, with 99 illustrations. Price, $4. Baltimore: William Wood & Company, 1937.

The chief merit of Ross Smith's new book on orthopedic surgery lies in its compactness and its usefulness to the rather large technical and lay organization built around the orthopedic surgeon. Members of such a group require a handy working reference, in order to become familiar with the more common orthopedic

conditions and procedures. The author, recognizing these needs, has added an appendix containing a brief résumé of the material on physical therapy, splints and appliances and technic of using plaster of Paris. Of interest also is a chapter on general considerations of fractures and one on the common injuries to nerves, muscles, tendons and joints.

The book is too limited in scope to be recommended seriously for medical students or practitioners.

**The Psychology of Exceptional Children. Vol. II.** By Norma V. Scheidemann, Ph.D. Pp. 460, with 33 illustrations and 16 tables. Price, $3.25. Boston: Houghton Mifflin Company, 1937.

It is the purpose of this textbook to present in an organized and systematic manner the accepted scientific findings in regard to several types of exceptional children, in order that the teacher may have a better comprehension of, and consequently be a better teacher for, these children.

The first chapter is devoted to the elementary anatomy of the nervous system; the second contains an excellent description of injury at birth and its problems, and the third takes up postencephalitic children. Chapter 4 describes some of the well known ideas on enuresis. The albinistic, "pre-schizophrenic" (whatever that is) child and the child afflicted with pubertas praecox are described. Chapters are devoted to premature, bilingual, eidetic and congenitally syphilitic children.

To a large extent the material represents a summary of the work of other authors, rather than of information gained from personal experience. The writer has carried out her purpose well in presenting the material for teachers. Being written for a lay group, the medical material is, of necessity, elementary.

**Die Diphtherie.** Edited by Prof. Dr. F. Hamburger. Price, bound, 16.50 marks; unbound, 16.00 marks. Pp. 280, with 53 illustrations, 5 in color. Berlin: Urban & Schwarzenberg, 1936.

The book is edited by Hamburger and consists of reviews by laboratory experts of the various points on epidemiology, bacteriology, toxin, toxoid, antitoxin, pathogenesis, pathology and pathologic anatomy and discussions by clinicians of the various types of diphtheria (nasal, aural, dermal, vulvar, etc.), the use of the electrocardiograph, prognosis, prophylaxis, therapy and serum sickness. The articles are well written and, although the review is comprehensive, it contains nothing that is new to American readers. One could hardly agree with the statement that tracheotomy predisposes to diphtheria septicemia. That the organisms of diphtheria are found in the myocardiums of a large percentage of persons suffering from diphtheria is a point that needs corroboration. The five colored illustrations are excellent. On the whole, the book is a good review of the current work on diphtheria.

**Pediatric Dietetics.** By N. Thomas Saxl. Price, $7. Pp. 565, with 57 plates and 89 tables. Philadelphia: Lea & Febiger, 1937.

The first section of this book is devoted to digestion in infancy and childhood, the second to the composition of foods, the third to the feeding of infants and the fourth to dietetic management of pediatric diseases. It is difficult to comment on a work of this kind beyond the statement that it contains exactly what the title says. The work necessary to complete such a book must have been enormous. The author discusses the feeding necessary for every type of pediatric condition imaginable. A list of the feedings given would be a list of all the pediatric diseases. The book is well written; the feedings given are excellent, and controversial points have been avoided. As a reference work this volume should be of great assistance to the general practitioner, as well as to the pediatrician.

# Obituary

## GEORGE H. SIMMONS, M.D.
## 1852-1937

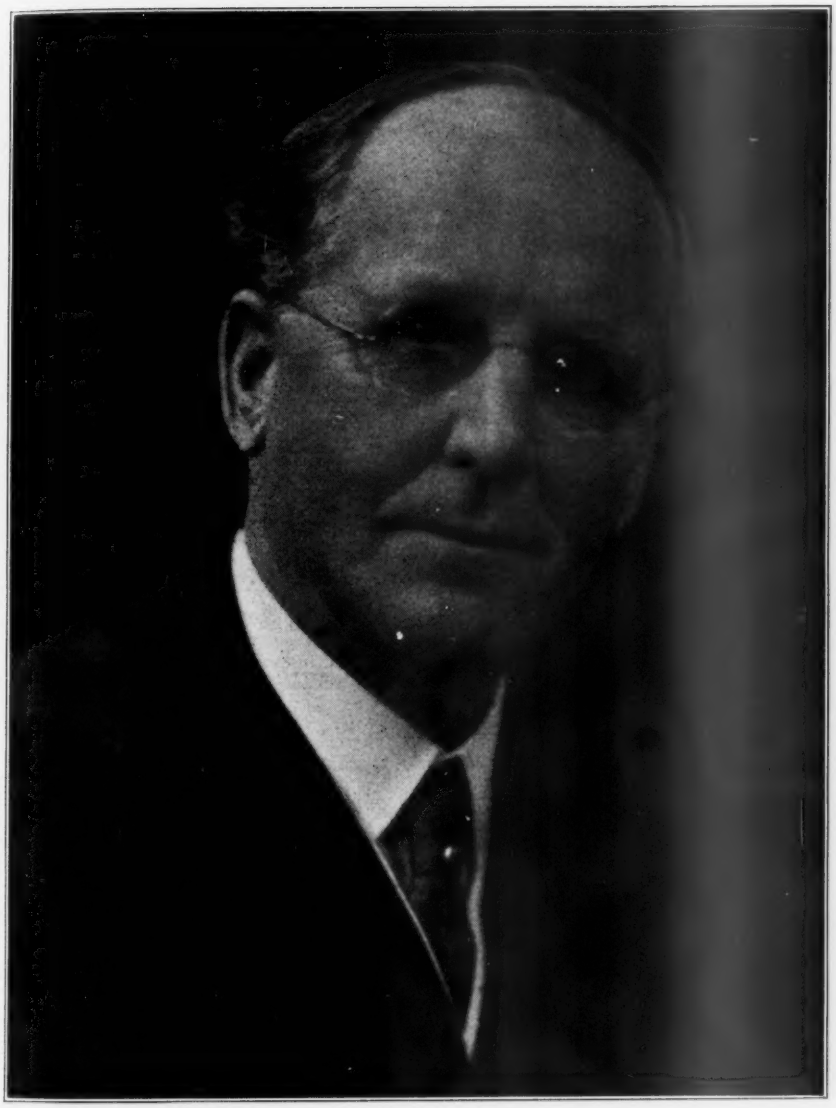
### DR. SIMMONS AND THE AMERICAN JOURNAL OF DISEASES OF CHILDREN

The passing of Dr. Simmons brings forcibly to attention the great interest which he took in the AMERICAN JOURNAL OF DISEASES OF CHILDREN. That Dr. Simmons had foreknowledge of a petition from a group of pediatricians for a journal on diseases of children which was presented to the Board of Trustees is not known. But it is a matter of record that he seconded the proposal heartily, on the ground that some papers read at the meetings of the sections of the American Medical Association were better fitted for a journal of this type and should be published earlier than was possible under the conditions which existed with respect to *The Journal of the American Medical Association.*

Dr. Simmons was always a great friend of the AMERICAN JOURNAL OF DISEASES OF CHILDREN and was proud of its success. Long before I was associated with the Editorial Board Dr. Simmons discussed with me at luncheon a program for the widening of the scope of the journal to provide for its greater usefulness. At the time Dr. Simmons was much disturbed because of the lack of material presented for publication and because of the small number of subscribers. Several years before the AMERICAN JOURNAL OF DISEASES OF CHILDREN assumed its present form Dr. Simmons was persuaded that it was desirable from many standpoints to include more than scientific papers in its pages; he, more than any one else, was responsible for the institution of the abstract department. On the many occasions when we met he always inquired about this journal and about the material which was being presented for it. He took a great interest in the abstract department and was apparently well pleased with its progress.

The passing of Dr. Simmons means more than the death of a great editor and a great organizer. It means the passing of a genius whose foresight and common sense directed many of the activities of the American Medical Association for years. It is a pleasure to feel that one of the publications in which he took much pride was the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

C. G. G.



GEORGE H. SIMMONS, M.D.
1852-1937

# Directory of Pediatric Societies *

## INTERNATIONAL

### International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Herreplein, Groningen, Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

### International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini 24, Rome, Italy.
Secretary: Professor Vitetti, Rome, Italy.
American Committee:
Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. L. Emmett Holt Jr., Johns Hopkins Hospital, Baltimore.
Canadian Committee:
Chairman: Dr. H. B. Cushing, 1390 Sherbrooke St., W., Montreal.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St., W., Montreal.

### International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.
Place: Rome, Italy. Time: Oct. 4-8, 1937.

## FOREIGN

### British Paediatric Association

President: Dr. J. Wilkie Scott, 40 The Rope Walk, Nottingham, England.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

### Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

### Royal Society of Medicine, Section for the Study of Diseases in Children

President: Sir Lancelot Barrington-Ward, 85 Harley St., London, W. 1.
Secretary: Dr. K. H. Tallerman, 122 Harley St., London, W. 1.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

### Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv, Palestine.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv, Palestine.

### Sociedad Cubana de Pediatría

President: Prof. Félix Hurtado Galtés, Carlos III 7, Havana.
Secretary: Dr. Carlos Hernández Miyares, San Lazaro 370, Havana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Havana. Time: Third Thursday of every month.

*Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

## NATIONAL

### American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Clifford D. Sweet, 2940 Summit St., Oakland, Calif.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: San Francisco. Time: June 13-17, 1938.

### American Academy of Pediatrics

President: Dr. Philip Van Ingen, 125 E. 71st St., New York.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Region I. Place: Boston, Mass. Time: Nov. 12-13, 1937.
Region II. Place: New Orleans, La. Time: Nov. 30-Dec. 1-3, 1937.
Region III. Place: Lake Shore Athletic Club, Chicago. Time: Oct. 14-16, 1937.
Region IV. Place: Los Angeles, Calif. Time: Nov. 4-6, 1937.

### American Hospital Association, Children's Hospital Section

Chairman: Miss Mabel Binner, Children's Memorial Hospital, Chicago.
Secretary: Winifred Culbertson, Children's Convalescent Hospital, Cincinnati.

### American Pediatric Society

President: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: The Sagamore, Bolton Landing, New York. Time: June 9-11, 1938.

### Canadian Society for the Study of Diseases of Children

President: Dr. Alton Goldbloom, 1543 Crescent St., Montreal, Quebec.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

### Society for Pediatric Research

President: Dr. Samuel Z. Levine, 525 E. 68th St., New York.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

## SECTIONAL

### North Pacific Pediatric Society

President: Frederick Fischer, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. C. L. Lyons, Paulsen Medical-Dental Bldg., Spokane, Wash.
Place: Seattle. Time: Last Saturday in January 1938.

### Southern Medical Association, Section of Pediatrics

Chairman: Dr. Gilbert Levy, 20 S. Dunlap St., Memphis, Tenn.
Secretary: Dr. Hughes Kennedy [illegible], Highland Plaza Apts., Birmingham, Ala.
Place: New Orleans. Time: Nov. 30-Dec. 3, 1937.

## STATE

### Alabama Pediatric Society

President: Dr. J. H. Baumhauer, 56 St. Joseph St., Mobile.
Secretary-Treasurer: Dr. M. Vaun Adams, 803 Government St., Mobile.
Place: Mobile. Time: Third Monday in April 1938.

### Arkansas State Pediatric Association

Chairman: Dr. E. C. McMullen, 500 Main St., Pine Bluff.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.
Place: Texarkana, Ark. Time: February 1938.

### California State Medical Society, Section on Pediatrics

Chairman: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.
Secretary: Dr. Hartzel H. Ray, 23–2d Ave., San Mateo.
Place: Pasadena. Time: May 9-12, 1938.

### Florida State Pediatric Society

President: Dr. Douglas D. Martin, 442 W. Lafayette St., Tampa.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Coral Gables.
Place: Concurrent with state association meeting at time of convention.

### Georgia Pediatric Society

President: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.
Place: Augusta. Time: April 1938.

### Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. J. Harold Root, 103 N. Main St., Waterbury.
Secretary: Dr. Joseph L. Hetzel, 103 N. Main St., Waterbury.
Time: Three meetings a year.

### Indiana State Pediatric Society

President: Dr. Ernest R. Carlo, 2902 Fairfield Ave., Fort Wayne.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

### Louisiana State Pediatric Society

President: Dr. Clarence H. Webb, 624 Travis St., Shreveport.
Secretary-Treasurer: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.
Place: New Orleans. Time: April 25-27, 1938.

### Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. John D. Craig, 33 E. 61st St., New York.
Secretary: Dr. Norman L. Hawkins, 11 Public Sq., Watertown, N. Y.
Place: New York. Time: May 9-12, 1938.

### Michigan State Medical Society, Pediatric Section

Chairman: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.
Secretary: Dr. Ward Chadwick, 524 Medical Arts Bldg., Grand Rapids.

### Mississippi State Pediatric Society

President: Dr. Guy C. Jarratt, 920 Cawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by Society. Time: Yearly.

### Nebraska Pediatric Society

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

### North Carolina Pediatric Society

President: Dr. John LaBruce Ward, Arcade Bldg., Asheville.
Secretary: Dr. Lewis Elias, 36 Grove St., Asheville.

### Oklahoma State Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. Ben H. Nicholson, 301 W. 12th St., Oklahoma City.

### Pennsylvania Medical Society, Pediatric Section

Chairman: Dr. Theodore O. Elterich, 3700–5th Ave., Pittsburgh.
Secretary: Dr. John M. Higgins, 600 S. Wilbur Ave., Sayre.
Place: Philadelphia. Time: Oct. 5-7, 1937.

### South Carolina Pediatric Society

President: Dr. Leland B. Salters, 317 S. Warley St., Florence.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

### Tennessee State Pediatric Society

President: Dr. Eugene Rosamond, 1074 Madison Ave., Memphis.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Nashville. Time: April 12-14, 1938.

### Texas Pediatric Society

President: Dr. John G. Young, 3930 McKinney Ave., Dallas.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Galveston. Time: May 10-12, 1938.

### Virginia Pediatric Society

President: Dr. W. Ambrose McGee, 616 W. Grace St., Richmond.
Secretary: Dr. John M. Bishop, Medical Arts Bldg., Roanoke.
Place: Danville, Va. Time: October 1938.

### West Virginia State Medical Society, Section on Pediatrics

President: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.
Secretary: Dr. Theresa O. Snaith, Weston.

## LOCAL

### Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Secretary: Dr. Arthur J. Horesh, 10515 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

### Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

### Bronx Pediatric Society

President: Dr. Daniel J. Dolan, 420 E. 159th St., New York.
Secretary: Dr. Samuel T. Levethan, 254 E. 184th St., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

### Brooklyn Academy of Pediatrics

President: Dr. Walter D. Ludlum, 1421 Cortelyou Rd., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

### Central New York Pediatric Club

President: Dr. Frank Vasder Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

### Chicago Pediatric Society

President: Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave., Chicago. Time: Third Tuesday of each month, October to May, inclusive.

### Dallas Pediatric Society

President: Dr. John Young, 3930 McKinney Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3622 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

### Detroit Pediatric Society

President: Dr. W. J. Scott, 5140–2d Ave., Detroit.
Secretary: Dr. Harold E. Clark, 100 Atkinson Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

### Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. T. F. Davenport, 104 Ponce de Leon Ave., Atlanta.
Secretary: Dr. James P. Hanner, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

### Houston Pediatric Society

President: Dr. Walter F. Qualtrough, 920 Westheimer Ave., Houston, Texas.
Secretary-Treasurer: Dr. Allan Penny Bloxsom, 4402 Travis St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

### Intermountain Pediatric Society

President: Dr. Eugene Smith, 385—24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 1020 Boston Bldg., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

### Kansas City (Missouri) Pediatric Society

President: Dr. W. R. Moore, 620 Francis St., St. Joseph.
Secretary: Dr. F. S. Hogue, 1103 Grand Ave., Kansas City.
Place: Kansas City General Hospital. Time: On call.

### Los Angeles County Medical Association, Pediatric Section

President: Dr. Edwin F. Patton, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

### Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Harry R. Litchfield, 163 Eastern Parkway, Brooklyn.
Secretary: Dr. Jacob Rosenblum, 550 Ocean Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

### Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. W. C. A. Steffen, 42 Union St., Flushing, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

### Memphis Pediatric Society

President: Dr. Clyde V. Croswell, 1052 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. David W. Goltman, 1073 Madison Ave., Memphis, Tenn
Place: John Gaston Hospital. Time: Quarterly.

### Milwaukee Pediatric Society

President: Dr. George F. Kelly, 425 E. Wisconsin St., Milwaukee.
Secretary: Dr. Helen Jane Zilmer, 781 N. Jefferson St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

### New England Pediatric Society

President: Dr. Henry E. Utter, 122 Waterman St., Providence, R. I.
Secretary-Treasurer: Dr. Henry E. Gallup, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meeting a year, occurring from September to May.

### New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Samuel Z. Levine, 525 E. 68th St., New York.
Secretary: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

### Northwestern Pediatric Society

President: Dr. Roger L. J. Kennedy, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Robert Rosenthal, 437 Lowry Medical Arts Bldg., St. Paul.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

### Oklahoma City Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Alternate months.

### Philadelphia Pediatric Society

President: Dr. Emily Bacon, 2104 Spruce St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

### Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

### Richmond Pediatric Society

President: Dr. Lee E. Sutton Jr., 2601 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. Louise Fry Galvin, 2416 Stuart Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

### Rochester Pediatric Society

President: Dr. J. Merrel Parker, 11 N. Goodman St., Rochester, N. Y.
Secretary: Dr. H. C. Soule, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

### Rocky Mountain Pediatric Society

President: Dr. James E. Russell Jr., 820 Metropolitan Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

### St. Louis Pediatric Society

President: Dr. John Zahorsky, 536 N. Taylor Ave., St. Louis.
Secretary-Treasurer: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

### Seattle Pediatric Society

President: Dr. Frank H. Douglass, Medical Dental Bldg., Seattle.
Secretary: Dr. C. Luverne Smith, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

### Southwestern Pediatric Society

President: Dr. Louis M. Earle, 6381 Hollywood Blvd., Los Angeles.
Secretary: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

### University of Michigan Pediatric and Infectious Disease Society

President: Dr. M. Cooperstock, Northern Michigan Children's Clinic, Marquette.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: University Hospital, Ann Arbor. Time: Nov. 19-20, 1937.

### Westchester County Medical Society, Pediatric Section (New York)

President: Dr. R. A. Higgons, 264 King St., Port Chester, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 131 Purchase St., Rye, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, October, December, February and April.